CONFABULATION AND MEMORY IMPAIRMENTS FOLLOWING FRONTAL LOBE LESIONS

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ABSTRACT

Neuroimaging studies have provided considerable evidence for frontal lobe involvement in memory processing. Memory impairments are also frequently reported in patients with frontal lobe lesions. However detailed anatomical localisation is rare, making integration of lesion and imaging findings difficult. An investigation of the functional and anatomical contributions of the frontal lobes to memory was conducted in 42 patients with frontal lobe lesions, examining memory processes identified in previous imaging and neuropsychological research. The results revealed frontal impairments in recall and recognition memory, increased false recognition and intrusions, and confabulation.

To investigate specific lesion-behaviour relationships, patients were grouped according to the presence of damage in Right Lateral, Left Lateral, Medial and Orbital frontal regions. The Medial group had impairments in recognition and recall on several tasks, which were due at least in part to deficits at encoding. This group may have a pure memory deficit arising from disruption of cholinergic projections from the basal forebrain to the medial temporal lobe system. The Right Lateral group on the other hand had a strategic retrieval deficit which was aided by cueing at recall. Marked intrusion and confabulation effects were found in the Orbital and Medial groups, providing strong support for an inferior medial localisation for confabulation.

In addition an investigation of Schnider and colleagues' theory of confabulation was conducted in three confabulating patients. Strong support was found for a characteristic pattern of performance on their continuous recognition task, with confabulators showing a constant hit rate accompanied by an increasing false positive rate. However the suggestion that the critical impairment is an inability to suppress currently irrelevant memories that intrude into the present was not supported. Instead these patients had a complete inability to place remembered information in its correct temporal context. There was also evidence of a tendency to misidentify imagined experiences as real. It is argued that retrieval process theories incorporating these factors are best able to account for the features of confabulation.

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CHAPTER ONE:
INTRODUCTION

1.1 MEMORY IMPAIRMENTS IN FRONTAL LOBE DAMAGE

Damage to the frontal lobes does not result in the kind of severe amnesic syndrome typical of lesions to the temporal or diencephalic structures. However there is now a large body of evidence suggesting that it may lead to a range of more subtle impairments of memory. These deficits are thought to be secondary to impairments in frontally located supervisory processes, rather than being pure memory deficits. "The frontal cortex is less involved in memory recollection per se, than it is in mediating the strategic processes that support memory encoding, recovery, monitoring and verification" (Moscovitch & Winocur, 2002, p188).

Impairments following frontal lobe lesions have been reported in a variety of memory tasks. Patients with frontal lobe damage have been reported to show deficits in working memory tasks (e.g. Owen, Sahakian, Semple, Polkey & Robbins, 1995) and in prospective memory (Shimamura, Janowsky & Squire, 1991). There is some evidence that frontal lobe damage may lead to abnormal sensitivity to interference (Moscovitch, 1982; Shimamura, Jurica, Mangels, Gershberg & Knight, 1995). Metamemory, the ability to make judgements and predictions about one's own memory abilities, has also been reported to be faulty amongst patients with frontal lobe lesions, who show less accurate "feeling of knowing" than normal controls (Janowsky, Shimamura & Squire, 1989a; Shimamura & Squire, 1986, Schnyer, Verfaillie, Alexander, LaFleche, Nicholls & Kaszniak, 2004; Vilkki, Servo & Surma-aho, 1998). However the most frequently reported memory deficits following frontal lobe damage are in tests of source and temporal memory, recall and recognition.

1.1.1 Source and Temporal Memory

Patients with frontal damage have frequently been reported to show deficits in memory for the source of information. Thus whilst item memory may be relatively preserved,

memory for contextual information about where and when the information was encountered is impaired. For example Janowsky, Shimamura & Squire (1989b) reported that although their frontal patients were able to recall factual information as readily as normal controls, they were impaired in their memory for the source of the information. They either reported that facts that were actually learned in an earlier experimental study phase had been learned from an outside source, or that facts previously known to them had been acquired as part of the experiment. Janowsky *et al* (1989b) concluded that this was the result of a disconnection between fact memory and context and proposed that "the frontal lobes are essential for associating information in memory to the context in which it was acquired" (Janowsky *et al*, 1989b, p 1055). Many findings in support of this hypothesis have been reported. For example Schacter, Harbluk & McLachlan (1984) reported that although frontal patients were able to recall fictitious facts taught to them in an experimental situation they could not recall which of two speakers had presented the information, and often reported that the facts had been learnt in a completely different context. Similarly, Shimamura, Janowsky & Squire (1990) asked frontal patients and controls to learn a series of answers to obscure quiz questions and reported that although the frontal patients had normal memory for the facts they could not recall their source, and frequently claimed that they had been learnt elsewhere. Further examples are provided by Ward & Parkin (2000) who reported that although their patient MR had a normal hit rate, he was impaired at identifying whether targets had previously been presented in picture or word form, Johnson, O'Connor & Cantor (1997) who reported that their confabulating patient GS and three other non-confabulating frontal patients were impaired at identifying which of two speakers had read target words to them, and Daum & Mayes (2000) who reported that their frontal group were impaired on a spatial memory task.

There is also strong evidence that patients with frontal lobe lesions have difficulty monitoring the temporal dimension of events in the past (e.g. Milner, Petrides & Smith, 1985), and this type of temporal context memory impairment has been specifically associated with dorsolateral prefrontal damage (Daum & Mayes, 2000; Fuster, 1985;

Kopelman, Stanhope & Kingsley, 1997b; Milner, Corsi & Leonard, 1991). Impaired performance has been reported in four types of task:

1) Recency Discrimination. Deficits in judging which of two items (words, pictures, or named objects) was presented most recently, in conjunction with normal item recognition, have been reported by Milner and colleagues (e.g. McAndrews & Milner, 1991; Milner *et al*, 1991; Milner *et al*, 1985). Similarly Kesner, Hopkins & Fineman (1995) reported that relative to controls patients with prefrontal cortex damage were impaired at judging which of two previously presented stimuli was presented earliest in a sequence, and Ward & Parkin (2000) reported that their patient MR was impaired at judging which of two words, pictures or actions had been presented (or performed) most recently.

2) Frequency Estimation. Smith & Milner (1988) reported that whilst their frontal patients were preserved at recognising previously presented abstract designs, they were impaired at estimating the frequency with which they had been presented. Similarly Stanhope, Guinan & Kopelman (1998) found that their frontal group were impaired compared to controls at frequency estimation and concluded that this was likely to be due to strategic difficulties in making an organised search in memory.

3) Temporal Sequencing. Shimamura *et al* (1990) found that their frontal group were impaired at reproducing the order of a recently presented word list, and at reproducing the chronological order of historical events. A similar deficit was reported in patient JB who was unable to put his own life events in the correct temporal order (Parkin, 1997).

4) List Discrimination. There are several reports that patients with frontal damage have difficulty judging which of two temporally distinguishable lists or sets an item was presented in. For example Butters, Kaszniak, Glisky, Eslinger & Schacter (1994) reported that frontal patients were impaired at identifying which of two sets an object had been presented in. Parkin, Leng, Stanhope & Smith (1998) reported that patient JB could not

recall which of two sets a previously presented sentence had been encountered in. Johnson *et al* (1997) reported that their frontal patients showed poor temporal order judgement when they were asked to identify which of two lists various stimuli (sentences, faces, words and abstract paintings) had been presented in. Similarly Daum & Mayes (2000) reported that their frontal group were at chance (54%) and significantly worse than controls at identifying which of two sets pictures of faces had been presented in.

The consistency of evidence relating problems with source and temporal information to prefrontal cortex pathology has led many to conclude that context memory for source and temporal order is dependent on frontal function (e.g. Schacter, 1987). However recent research has revealed that the relationship between source memory and frontal functioning may not be so straightforward. Kopelman *et al* (1997b) reported that their patients with frontal lesions performed at the same level as controls on a spatial context memory task when they were asked to identify whether a drawing had been presented at the top or bottom of a flashcard. They also found that only 3 out of 15 patients (interestingly the only three with dorsolateral frontal damage) were impaired at making temporal judgements regarding which of two blocks the pictures had been presented in. The remaining 12 patients with medial lesions not encroaching upon the dorsolateral region were unimpaired. One clue to the discrepancy in these results may come from the fact that participants in the Kopelman *et al* (1997b) study were explicitly instructed to remember spatial and temporal information about the pictures, where in most previous studies participants were only directed to remember the target items, meaning that any encoding of source was incidental. Thaiss & Petrides (2003) again explicitly instructed their participants to remember information about the source of facts learned whilst watching a video of a game show. Participants were required to remember not only the facts themselves but also which of three game show contestants had given them, and in another condition, which of three sections of the game show the facts had been encountered in. They found that their frontal patients were not impaired on either source or temporal memory judgements. They concluded that if source information is encoded explicitly, then the frontal cortex is not necessary for its retrieval; instead the frontal lobes would come into play when context is not explicitly encoded and strategic retrieval

processes are then required to retrieve contextual information. It is hypothesised therefore that the prefrontal cortex does not represent or store any specific form of source or temporal memory itself (that is the role of the hippocampus) but that it is involved in the on line control of memory retrieval operations including those relating to source information. Source recollection places particular demands on executive control compared to item memory, e.g. selecting, maintaining, updating and rerouting information, and thus is particularly susceptible to disruption following frontal damage (Moscovitch & Winocur, 1995; Shimamura, 2002).

1.1.2 Tests of Recall and Recognition

Frontal lobe lesions may also result in impairments on more traditional memory tasks including recall and recognition tasks. Recall tasks are likely to be effortful, requiring the participant both to initiate an effective search in memory and to evaluate the products of this search, and are likely to make greater use of contextual information and conscious recollective processes. As such, they should require more mediation by supervisory process located in the frontal lobes than recognition tasks, which are assumed to also involve relatively automatic processes based on familiarity. If the memory impairments observed following frontal damage are secondary to deficits in executive control processes overseen by the frontal lobes, one would expect to see the greatest impairment in free recall tasks, and the least impairment in recognition tasks. If on the other hand the impairments arise from a disruption in core memory processes, affecting the ability to store information, patients should be equally impaired on both tasks. In keeping with the memory control process hypothesis, the majority of the evidence suggests that the greatest impairments amongst patients with frontal lobe damage are found in free recall tasks, with more moderate impairments in cued recall, and the least disruption being evident in recognition tasks (Wheeler, Stuss & Tulving, 1995).

Janowsky, Shimamura, Kritchevsky & Squire (1989) and Shimamura *et al* (1991) found a disproportionate impairment on tests of free recall amongst their frontal patients, whilst recognition was unimpaired. Similarly Dimitrov, Granetz, Peterson, Hollnagel, Alexander & Grafman (1999) and Jetter, Posner, Freeman & Markowitsch (1986)

reported particular deficits in free recall, and attributed this to impairments in the use of effortful retrieval strategies. This recall deficit appears to apply to a wide range of stimuli, for example Daum & Mayes (2000) reported frontal deficits in recall of stories, word lists and dot patterns. Similar deficits have been observed in the recall of personal autobiographical information (Della Sala, Laiacona, Spinnler & Trivelli, 1993; Kopelman, Stanhope & Kingsley, 1999). Parkin, Yeomans & Bindschaedler (1994) for example reported that their patient CB had great difficulty producing detailed autobiographical memories in response to single word cues. For the cue "flower", he was only able to produce the response "I like flowers".

Most authors have attributed the recall impairments of frontal patients to difficulties in employing effective strategies at encoding or retrieval. For example, Kopelman & Stanhope (1998) reported that their frontal group differed from amnesic patients in that they showed an improvement in recall if semantically organised rather than unrelated word lists were used, hence externally providing the organisation that they were unable to impose subjectively. Incisa della Rochetta (1986) gave patients with frontal and temporal lesions pictures of common objects that they had to arrange into groups before later attempting to freely recall as many of the items as possible. Both groups did poorly in the recall task, but whilst the group with temporal excisions showed no deficits in categorising the pictures, the group with frontal excisions showed a significant deficit in categorisation, being unable to create appropriate categories, and leaving many items uncategorised. Whilst the right frontal group's recall impairment was associated mainly with this categorisation impairment at encoding, the left frontal group seemed also to have disrupted retrieval strategies causing an inadequate search in memory.

Several other groups have reported similar results. Gershberg & Shimamura (1995) found that their subjects benefited from strategy instructions at the study stage and at the test stage, implying that deficits in implementing organisational strategies at encoding and in implementing strategic processes at retrieval were to blame for their poor recall performance. Hirst & Volpe (1988) and Eslinger & Grattan (1994) concentrated on the encoding stage, noting that frontal lobe damaged patients tend not to spontaneously

categorise word lists or use other top-down processes to aid encoding. Others have highlighted strategy deficits at retrieval, either in poor subjective organisation measured by pair frequency (Vilkki *et al*, 1998) or in improved recall when retrieval cues are externally provided (Incisa della Rochetta & Milner, 1993), especially amongst left frontal patients.

Hanley, Davies, Downes & Mayes (1994, see also Hanley, Davies, Downes, Roberts, Gong & Mayes, 2001), for example, reported a patient with a lesion in the left caudate nucleus following rupture and repair of an anterior communicating artery aneurysm (ACoA). He was able to perform completely normally on recognition tasks. However he was severely impaired at freely recalling a short story, and also showed impoverished performance when his recall was cued on a paired associate learning task. His free recall deficit was not aided by providing instructions at the study stage, implying that he was able to encode normally, but that his retrieval processes were faulty. Hanley *et al* (1994) therefore concluded that his frontal damage had produced a selective deficit in initiating memory search processes. Whilst providing external cues in the paired associate task went some way to overcoming his deficit, free recall was severely impaired.

Diamond DeLuca & Kelley (1997) used the Rey-organisational and extended memory procedure to examine whether the visual memory impairments observed in their group of ACoA patients were due to inadequate encoding, accelerated levels of forgetting, or retrieval failure. They reported that their 6 amnesic ACoA subjects seemed to comprise two subgroups. In one, immediate recall could be improved to the level of the nonamnesic ACoA group by providing an organisational strategy for encoding. Encoding deficits, perhaps mediated by executive dysfunction, seemed to underlie the memory deficit in this group. The other subgroup were not helped by organisational procedures at encoding, but their pattern of impaired recall with preserved recognition, spatial discrimination and spatial assembly implied that their deficit was due to impaired retrieval processes. Forgetting and consolidation seemed to be normal in both groups.

Most studies have included a wide variety of aetiologies in their "frontal" groups. Whilst some used mainly dorsolateral lesions, others have used ACoA patients who frequently have more severe memory problems arising from ventromedial damage (see section 1.2.5) Furthermore most studies have used a single undifferentiated "frontal" group or created subgroups of only left or right frontal damage. Two recent studies have employed rather more sophisticated functional lesion localisation techniques to assess whether different deficits might follow lesions to different subregions of the frontal lobe.

Stuss, Alexander, Palumbo, Buckle, Sayer, & Pogue (1994) studied the performance of 32 patients with focal frontal lesions on a list learning task. They reported a general impairment in recall that was due to an inability to impose a higher order subjective organizational structure to assist word list learning. There were also two specific effects limited to particular regions of the prefrontal cortex. Those patients with left frontal damage had an additional secondary memory impairment due to mild language deficits, and those with right frontal damage produced excess extra-list repetitions in their recall, indicating poor checking and monitoring processes. More recently Alexander, Stuss & Fansabedian (2003) extended these results, reporting that patients with posterior left dorsolateral or posterior medial frontal lesions had the most marked deficits in free recall. The left posterior dorsolateral deficit appeared to arise from a mild lexical semantic deficit whilst the medial impairment was attributed to a more direct disruption of the memory system arising from the loss of cholinergic projections to the hippocampus.

The recall deficit amongst frontal patients, although the specific impairment may vary according to lesion site, is well established. The supposed preservation of recognition memory abilities (Hanley *et al*, 1994; Janowsky *et al*, 1989, Jetter *et al*, 1986; Milner *et al*, 1991, Shimamura *et al*, 1991; Stuss & Benson 1984) however has more recently come into question. Kopelman & Stanhope (1998) have argued that the differences observed between recall and recognition may be due to ceiling effects in recognition performance. When they matched recognition performance they found no disproportionate recall impairment in their frontal group, raising the possibility that some patients may have an equal recall and recognition deficit when task difficulty is equated.

Mayes & Daum (1997) also reported impaired word recognition performance in their frontal group, Daum & Mayes (2000) found impaired recognition for words and faces, Delbecq-Derouesne, Beauvois & Shallice (1990) reported a patient with impaired recognition but preserved recall, Dimitrov *et al* (1999) reported a mild recognition deficit in their frontal group, and Schnyer *et al* (2004) found that their frontal patients were less accurate at recognising the final missing word in a set of previously learned sentences. Stuss *et al* (1994) attempted to identify the mechanisms of the unexpected recognition deficit in their unilateral left and bifrontal groups and found that on closer examination patients with impaired recognition could be divided into two groups. One group had lesions extending into the septal region or posterior extent of the anterior cingulate, maybe producing a mild form of amnesia due to damage to the limbic structures necessary for explicit memory. The other had mild language impairment resulting from left frontal pathology (dorsolateral striatal or superior medial) which was argued to result in a verbal encoding deficit. Wheeler *et al* (1995) in their review found that in 18/21 studies frontal patients performed worse than controls in recognition tasks. It appears that in some cases frontal injury may impair even simple recognition.

1.1.3 Pathological False Recognition

One particular source of error on recognition tasks that is frequently reported is a pathologically high rate of *false* recognition – in which subjects produce abnormally high levels of false alarms with a normal hit rate. Schacter and colleagues (Curran, Schacter, Norman & Gallucio, 1997; Schacter, Curran, Gallucio & Milberg, 1996) have described a patient, BG, with infarction of the posterior aspects of the right frontal lobe, who showed a normal hit rate, but made an excessive number of false alarms on recognition tests with a variety of stimuli (words, sounds, pictures and pseudowords). Furthermore, his false responses were accompanied by "remember" rather than "know" responses, indicating a recollective experience rather than a response based simply on familiarity. Although his false recognition was robust, it was ameliorated if targets and distractors were drawn from different taxonomic categories. This pattern of performance suggests that his false recognition was due to a deficit at the retrieval stage, in that he appeared to have too

liberal a response criterion, allowing many items to be accepted unless targets and distractors were clearly different in some way. Delbecq-Derouesne *et al* (1990) concluded that a retrieval deficit was also responsible for RW's high false recognition rates, in which he was unable to distinguish between familiarity arising from a memory of having experienced the target previously, and familiarity aroused by an associative response when encountering a distractor.

Pathological false recognition with high confidence has also been described by Parkin and colleagues (Patient JB, Parkin, Bindschaedler, Harsent & Metzler, 1996; Parkin, Ward, Bindschaedler, Squires & Powell, 1999; Patient MR, Ward & Parkin, 2000. In both cases, false alarm rates were not affected by manipulations at retrieval, however performance could be improved by carrying out a semantic orienting task at study. Parkin *et al* (1999) and Ward & Parkin (2000) argued therefore that the false recognition in these patients arose from an encoding deficit in which poorly focused memory descriptions of the target items were formed which lacked item specific information but instead contained features common to many items, including distractors. It is interesting that these patients had left sided lesions, in contrast to BG and RW whose lesions were predominantly right sided.

Group studies have also found high rates of false recognition in patients with frontal lobe lesions. Melo, Winocur & Moscovitch (1999) reported that nonamnesic frontal lobe patients produced elevated levels of false recognition. They concluded that this was due to an inability to monitor their memory retrieval or to retrieve contextual information to verify the products of their memory search. These patients therefore accepted memories as veridical based on general gist. Swick & Knight (1999) used a continuous recognition procedure and found that their (mainly left dorsolateral) frontal patients showed a normal hit rate with an elevated false alarm rate. They too attributed this to an impairment in the use of source monitoring strategies at retrieval to establish the basis of familiarity. Verfaillie, Rapscak, Keane & Alexander (2004) found elevated false alarm rates in their amnesic frontal group, but also reported that several nonamnesic frontal patients had increased false alarm rates with a normal hit rate, assumed to be due to impaired

monitoring and verification. Budson, Sullivan, Mayer, Daffner, Black & Schacter (2002) also reported that their frontal lobe damaged and Alzheimers groups showed elevated level of false recognition across 5 study-test trials of lists of semantic associates, whilst controls were able to reduce their false recognition. They concluded that the frontal lobes enable normal memory function by suppressing false recognition and other memory distortions via monitoring and verification of where a sense of familiarity is arising from. Their argument is similar to Shimamura's dynamic filtering theory (Shimamura, 1995, 2000, 2002) in which the prefrontal cortex monitors and controls memory processing by inhibiting certain activations and maintaining others.

False recognition amongst frontal patients is an established phenomenon. However the critical lesion site is less clear. Schacter, Norman & Koutstaal (1998) have argued that it is associated with ventromedial and posterior frontal lobe damage, and this is the case with patients RW, JB and BG. But there are also several reports of false recognition following left dorsolateral damage (Alexander *et al*, 2003; Swick & Knight, 1999). As with all the "frontal" memory impairments reported so far, further research is needed to pinpoint the exact areas of damage that trigger increased false recognition.

A different type of false recognition, specific to faces, has been described by Rapcsak and colleagues (Rapcsak, Nielsen, Littrell, Glisky, Kaszniak & Laguna, 2001; Rapcsak, Polster, Comer & Rubens, 1994; Rapcsak, Polster, Glisky & Comer, 1996; Rapcsak, Reminger, Glisky, Kaszniak & Comer, 1999) in a series of patients with right frontal lobe damage. These patients display a tendency to say that faces they have never seen before are familiar which is not explicable by a simple loss of memory for faces. However if they are instructed to try to recall the context in which they experienced the face, they are able to suppress this false recognition. Rapcsak *et al* (1999) therefore conclude that the phenomenon arises from a retrieval deficit in which patients fail to engage strategic monitoring and criterion setting processes critical for attributing familiarity to a specific source. Ward, Parkin, Powell, Squire, Townshend & Bradley (1999) have also reported that their patient, MR, has a strong tendency to falsely recognise unknown faces as famous. They concluded that his retrieval description is too broadly specified so he

retrieves both relevant and irrelevant (erroneous) information. Rather than posit a monitoring explanation, they argue that his failure to inhibit (Moscovitch, 1995, 2000, 2002) or stop retrieval (Papagno & Baddeley, 1997) leads to his false recognition.

Commission errors may be observed in more extreme forms outside structured recognition tasks. For example patients with frontal lobe damage have frequently been reported to spontaneously intrude items in recall that were not initially presented to them (e.g. Baldo, Delis, Kramer & Shimamura, 2002; Daum & Mayes, 2000; Delbecq-Derouesne *et al*, 1990; Mayes & Daum, 1997; Melo *et al*, 1999). However, the most striking manifestation of false memory associated with frontal pathology is to be found in confabulation.

1.2. CONFABULATION

1.2.1 Characteristics of Confabulation

Confabulation has been defined as "a falsification of memory occurring in clear consciousness in association with an organically derived amnesia" (Berlyne, 1972), and was first used to describe the false statements made by patients with Korsakoff's amnesia in the acute stage of their illness. However it has now been reported in association with a variety of aetiologies including Korsakoff's syndrome (Dalla Barba, Cipolotti & Denes, 1990; Mercer, Wapner, Gardner & Benson, 1977; Talland, 1965), Alzheimer's disease (Kern, van Gorp, Cummings, Brown & Osato, 1992), following sub-arachnoid haemorrhage and rupture of anterior communicating artery aneurysms (Damasio, Graff-Radford, Eslinger, Damasio & Kassell, 1985b; Delbecq-Derouesne *et al*, 1990; Kapur & Coughlan, 1980; Kopelman Guinan & Lewis, 1995; Moscovitch, 1989, 1995; Stuss, Alexander, Lieberman & Levine, 1978), tumour (Fotopolou, Solms & Turnbull, 2004), herpes simplex encephalitis (Del-Grosso-Desteri, Farina, Calabrese, Pinardi, Imbomone & Mariani, 2002) and following head injury (Baddeley & Wilson, 1988; Burgess, Baxter, Rose & Alderman, 1996; Demery, Hanlon & Bauer, 2001). Interestingly, the common denominator in these conditions appears to be the presence of frontal or adjacent damage.

Confabulation involves false beliefs that are often held with considerable conviction, are believed to be true memories and are not intended to deceive the listener. Moscovitch (1989) has therefore described it as "honest lying". The content of these statements may range from subtle alterations of true events, where real recollections are miscombined or placed in the wrong temporal or other context, to implausible reports of episodes that are bizarre and internally inconsistent. In extreme cases, confabulations may also be associated with an attempt to act upon the mistaken belief. It is frequently accompanied by anosognosia and a lack of awareness of the inaccuracy or absurdity of the beliefs, and the beliefs are often very resistant to contrary evidence. Whilst they tend to be verbal, possible visual confabulation has been reported (Downes & Mayes, 1995, patient NH)

Moscovitch (1995) has listed the defining features of confabulation, drawing on Talland (1965):

1) They are usually verbal statements but may also be non-verbal depictions or actions.
2) Typically they concern the patient but may also include non-personal information such as historical events, fairy tales (Delbecq-Derouesne *et al*, 1990; Luria, 1976), geography (Moscovitch, 1989), and other aspects of semantic memory (Dalla Barba, 1993b).
3) The account need not be coherent and internally consistent.
4) The account is false in the context in which it is related and often false in details within its own context.
5) Most often the account is drawn from recollection of the patient's own experiences, including his thoughts in the past and current musings.
6) Information is presented without awareness of its distortions or of its inappropriateness, and without concern when the errors are pointed out.
7) Usually confabulation serves no purpose and is motivated in no other way than by the patient's attempt to relate his experiences. Initial confabulations are not produced to oblige the listener or to fill in gaps in the patient's knowledge (cf. Talland, 1965) although secondary confabulation may be produced to explain the internal inconsistencies of the primary confabulation.

8) Readiness to confabulate may be determined by the patient's "personality structure, the traits evolved in dealing with the environment and in monitoring his image" (Talland, 1965, p44)

1.2.2 Momentary and Fantastic, Spontaneous and Provoked Confabulation

Berlyne (1972) followed Bonhoeffer (1904) in distinguishing between two types of confabulation – "momentary" and "fantastic" confabulation. The momentary type describes fleeting confabulations, provoked by questions probing the subject's memory, and consisting of real memories displaced in temporal context. Fantastic confabulation on the other hand describes spontaneously produced, sustained, wide-ranging and grandiose beliefs, evident in the subject's everyday conversation. Kopelman (1987, 1999) has more recently proposed a slightly different distinction between "provoked" and "spontaneous" confabulation, which avoids confounding the eliciting conditions of confabulation with its content. "In "spontaneous" confabulation there is a persistent, unprovoked outpouring of erroneous memories, as distinct from "momentary" or "provoked" confabulation, in which fleeting intrusion errors or distortions are seen in response to a challenge to memory, such as a memory test" (Kopelman, 1999).

The characteristics of confabulation are best illustrated with examples. The following example is provided by Moscovitch (1995) and is an extract from an interview with HW, a patient who suffered rupture and repair of an anterior communicating artery aneurysm.

"Q: Can you tell me a little bit about yourself? How old are you?
A: I'm 40, 42, pardon me, 62.
Q: Are you married or single?
A: Married.
Q: How long have you been married?
A: About 4 months
Q: What's your wife's name?
A: Martha
Q: How many children do you have?
A: Four. (He laughs). Nor bad for four months!
Q: How old are your children?

A: The eldest is 32, his name is Bob, and the youngest is 22, his name is Joe.

Q: How did you get these children in four months?

A: They're adopted.

Q: Who adopted them?

A: Martha and I.

Q: Immediately after you got married you wanted to adopt these older children?

A: Before we were married we adopted one of them, two of them. The eldest girl Brenda and Bob, and Joe and Diana since we were married.

Q: Does it all sound a little strange to you, what you are saying?

A: (He laughs). I think it is a little strange.

Q: Your record says that you've been married for over 30 years. Does that sound more reasonable to you?

A: No.

Q: Do you really believe that you have been married for 4 months?

A: Yes."

This excerpt is an example of provoked confabulation and clearly shows HW's temporal confusion. Whilst the information he is recalling is largely correct, he is recalling it in the wrong temporal context. In an attempt to resolve the inconsistencies in his account, he then goes on to provide further confabulatory details, which he is convinced of, despite realising how odd they sound.

An example of more fantastic or bizarre confabulation is provided by Damasio *et al* (1985b). They report a patient who following a ruptured anterior communicating artery aneurysm confabulated that he was a spaceship commander at the time of the Columbia space mission, during which time he occasionally became a "space pirate". His confabulations were accompanied by vivid visual descriptions and held with considerable conviction. Interestingly, Damasio *et al* (1985b) include an excerpt from an interview with this patient 5 weeks after the onset of his illness, when the worst of his confabulation had resolved:

"Q: You had some peculiar ideas during your admission here. Can you tell us about some?

A: I was a pirate and I commanded a spaceship (embarrassed laughter). Now I realise it's not true. I *didn't* dream that; it was a total part of consciousness. To me, it was reality at that time. It's

embarrassing now. At times, even reality is a dream. It was continuous throughout the day. I did believe it!"

This excerpt gives some insight into the subjective experience of his confabulation, and the gradual return of awareness. A similar example is provided by Joseph (1988) who described a janitor who, following a large right frontal subdural haemotoma, confabulated that he was the owner of the business where he previously worked. He also claimed to be a congressman and fabulously wealthy. He sometimes said that he realised what he was saying was probably not true "and yet I feel it and believe it though I know it's not right".

1.2.3 Confabulation in Episodic and Semantic Memory

Confabulation occurs most frequently in autobiographical or episodic memory recall. However there is evidence that in more rare cases it may also be observed in semantic memory (Baddeley & Wilson, 1986; Dalla Barba, 1993a,b; 1995; Fotopolou *et al*, 2004; Kopelman, Ng & Ven Den Brouke, 1997a; Moscovitch & Melo, 1997; Nedjam, Dalla Barba & Pillon, 2000).

Dalla Barba (1993a,b, 1995) describes 2 confabulating patients. Patient MB performed poorly on memory tests, but his performance on tests sensitive to executive function was relatively preserved. Patient SD had impaired performance on both memory and executive tests, and also had impaired semantic knowledge. Dalla Barba devised a "confabulation battery", consisting of 95 questions probing different types of information – personal semantic, general semantic, linguistic semantic, episodic, orientation in time and place, and questions that would elicit an "I don't know" response from normal subjects in both the semantic and episodic domains. Whilst MB confabulated only in response to questions probing episodic memory, orientation for time and place, and personal semantic memory, SD produced fantastic confabulation that was elicited by every type of question. Dalla Barba therefore concluded that confabulation will be found in the same memory domains that are deficient. Therefore SD's impaired semantic knowledge gave rise to his semantic confabulation. Semantic memory impairment in

combination with semantic confabulation has also been noted by Baddeley & Wilson (1986, patient RJ).

This argument has not been universally accepted. Moscovitch & Melo, 1997, for example have argued that the greater incidence of confabulation in the episodic domain reflects the greater demands that recall from episodic memory makes on frontally located memory control processes compared to recall from semantic memory (this argument is elaborated later). However it is now accepted that confabulation is not restricted to the episodic domain, and theories attempting to account for confabulation must therefore explain semantic confabulation as well.

1.2.4 Mechanisms of Confabulation: A Role for Frontal Dysfunction?

Confabulation has in the past been attributed to suggestibility (Berlyne, 1972) or psychological defence mechanisms (Weinstein & Kahn, 1955; Gainotti, 1975). However these accounts fail to adequately explain the characteristics of confabulation. Why are confabulations sometimes spontaneously offered, and why do some patients continue to believe in them despite evidence to the contrary? Some of the earliest theories attributed confabulation directly to memory impairment, by arguing that patients were compensating for their faulty memories by filling in the gaps in their knowledge with invented information (Bonhoeffer, 1901, cited in Talland, 1965; Barbizet, 1963). However confabulation is relatively uncommon, and is not seen in classical amnesia arising from diencephalic or medial temporal lobe damage. Memory impairment alone therefore cannot be sufficient to produce confabulation. In fact most amnesic patients, and many patients with frontal damage, simply respond that they do not know or cannot remember lost information when questioned (e.g. Dalla Barba, 1993a; Papagno & Muggia, 1996). There are also several studies indicating that the degree of memory loss does not correlate with the presence of confabulation (Mercer *et al*, 1977; Kapur & Coughlan, 1980; Stuss & Benson, 1984). Something else must be the key mechanism.

During the 1970s it began to be noted that confabulation was frequently associated with frontal dysfunction (Luria, 1976). As noted earlier it is associated with aetiologies that

tend to involve frontal dysfunction as well as memory impairment, for example Korsakoff's syndrome, Alzheimer's disease, and anterior communicating artery aneurysms. It also tends to be associated with performance on cognitive tests sensitive to frontal lobe damage (Stuss & Benson, 1986; Stuss *et al*, 1978; Baddeley & Wilson, 1986; Kopelman, 1987; Kapur & Coughlan, 1980; Mattioli, Miozzo, & Vignolo, 1999). Although some have suggested that confabulation may result from executive dysfunction alone (Benson & Stuss, 1990; Johnson 1991; Joseph, 1986) it is generally agreed that some degree of memory impairment (although not global amnesia) is also necessary. The idea that confabulation is caused by amnesia overlaid with a dysexecutive syndrome has therefore become very popular (Baddeley & Wilson, 1986; 1988; Cunningham, Pliskin, Cassisi, Tsang & Rao, 1997; Kapur & Coughlan, 1980; Kopelman, 1987; Mercer *et al*, 1977; Shapiro, Alexander, Gardner & Mercer, 1981).

So how might frontal dysfunction give rise to confabulation? As early as 1967, Luria, Homskaya, Blinkou & Critchley made reference to memory control processes in their description of a confabulating patient. They attributed his confabulation and intrusions to a "loss of matching of relevant and irrelevant associations which is so important a component of any selective process of memorisation" (p 110). Several proposals have been made as to the exact memory control processes that may be impaired in confabulation.

Stuss *et al* (1978), for example, reported five cases of spontaneous, fantastic confabulation, each with a lesion in the frontal lobe. They concluded that in addition to amnesia, frontal lobe dysfunction causing failure to inhibit responses, inability to monitor behaviour, misuse of environmental cues, a tendency to be impulsive, and lack of concern about incorrect performance, was necessary to produce persistent and spontaneous confabulation. Mercer *et al* (1977) reported that in memory questioning, confabulators tended to respond quickly, to correct themselves less often than other patients, and to use cues only intermittently as an aid to responding. They therefore proposed a model of the mechanisms of confabulation, which they believed arose when 1) the subject believed that a response was required, 2) an accurate memory of the answer was lacking due to

memory impairment, 3) an over-learned and affectively significant response was available, and 4) their ability to monitor or self-correct was defective.

Shapiro *et al* (1981) reported that the use of highly structured cues could reduce the number of confabulatory intrusions produced by their confabulating patients on a visual recall test, implying that a deficit at the retrieval stage was producing these subjects' errors. They concluded that confabulation was most associated with perseveration of an inappropriate response set, and that impaired self-monitoring and a failure to inhibit incorrect responses were also involved. Baddeley & Wilson (1986, 1988) also concluded that confabulation arises from a dysexecutive syndrome that disrupts the process of recollection. They argued that the active and problem-solving components of autobiographical retrieval are impaired, leading to problems in setting up retrieval cues for an effective search in memory, and in evaluating the information that is retrieved for whether it is veridical and matches the sought-after information. This, they argued, in combination with a clouding of autobiographical memory due to memory impairment, leads to confabulation.

Papagno & Baddeley (1997), in their description of patient MM, proposed that confabulation might arise not from a failure to provide correct information, but a failure to *stop* providing information, which led him to go on to give confabulatory details. They explained this aspect of his behaviour by recourse to "Stop rules" (Rundus, 1973; Shiffrin, 1970), which describe the normal awareness that retrieval is becoming unreliable, and tell us to stop. They argued that MM appeared to have a relatively adequate memory capacity, but could not evaluate what he was retrieving, and stop this retrieval process when it became implausible. Similarly Papagno & Muggia's (1996) patient MB was assumed to confabulate as a result of impaired self-monitoring in conjunction with a failure to inhibit incorrect responses. They argued that whilst a severe memory impairment would have prevented confabulation, the presence of fragmentary remembrances in combination with a dysexecutive impairment would elicit them.

Kopelman *et al* (1997b) highlighted specific impairments in source memory in their explanation for the florid confabulation of their Korsakoff's patient AB. She exhibited spontaneous confabulation extending across episodic, personal semantic and general semantic memory, mistaking doctors and researchers for family or friends, and believing that she was in the hospital where she used to work. The authors concluded that confusion in the context of her memories, perseveration and a tendency to respond indiscriminately to the immediate social and environmental context contributed to her confabulation. Similarly Downes & Mayes (1995) argued that an inability to monitor the source of experiences was responsible for confabulation, allowing patients to accept dreams and imaginings as real experiences.

Damasio, Eslinger, Damasio, Van Hoesen, & Cornell (1985a) have suggested that memory deficits may arise from a "modal mismatching effect", where patients are able to store the individual components of experiences, but are unable to integrate them. They argue that contextual (temporal or spatial) bonds between memory fragments are not established, and patients are then unable to cross-index between different aspects of the same event memory. An inability to tag events in this way may give rise to confabulation when fragments of disparate memories are conflated inappropriately.

All of these investigators therefore attribute confabulation to impairments in frontally located control processes, either directly or indirectly involved in the mnestic domain, which in some way allow the emergence of false memories in the presence of a memory impairment. These candidate processes include general attentional and motivational failure, a tendency to be impulsive or perseverative, a lack of concern about correct performance, a misuse of environmental cues or inability to set up appropriate retrieval cues, a failure to inhibit incorrect responses or stop memory search, a failure to use contextual information, and an inability to accurately monitor or evaluate behaviour or memories. In each case, the process, not the memory itself, is seen as the key impairment.

Cases in which confabulation is present in the absence of deficits on tests of executive function pose a problem for theories which highlight the role of frontally located memory

control processes in confabulation. Delbecq-Derouesne *et al* (1990) for example reported a patient RW who, following rupture and repair of an anterior communicating artery aneurysm, performed normally on all tests of frontal function except for letter fluency. Similarly, Dalla Barba *et al* (1990) reported a Korsakoff's patient CA who exhibited provoked confabulation with preserved performance on executive tests, and Papagno & Muggia's (1996) meningo-encephalitic carcinomatosis patient MB also showed preserved performance on frontal tasks. There are two possible explanations for this pattern of performance. Firstly, it may be that patients who display a milder degree of confabulation are likely to be less impaired on frontal / executive tests (DeLuca & Cicerone, 1991; Kapur & Coughlan, 1980; Kopelman, 1987; Shapiro *et al,* 1981; Stuss *et al*, 1978). Secondly, it may be that frontal pathology is present but not affecting performance on the particular tests chosen. Cunningham *et al* (1997), for example, reported that confabulation was related to tests tapping sustained attention, set-shifting and mental tracking, but not concept formation, problem-solving or verbal fluency. Moscovitch & Melo (1997) propose that the brain areas involved in confabulation and frontal test performance may be adjacent but not overlapping. Typically, damage will affect both areas and result in a dual impairment, but damage may occasionally be restricted to one area or the other and produce only one impairment. Certainly poor performance on executive tests even in combination with a memory impairment is not sufficient to produce confabulation. It may also be that it is not a necessary feature. A more problematic case for the frontal hypothesis of confabulation is presented by Dalla Barba, Boisse, Bartolomeo & Bachoud-Levi, (1999), whose posterior communicating artery aneurysm patient displayed confabulation and impairments on executive tests in the absence of frontal pathology. Whilst this pattern is certainly interesting and deserves further study, the fact remains that the majority of reported cases of confabulation involve frontal pathology, and this involvement requires explanation.

1.2.5 The ACoA Syndrome

Before moving on to discuss current theories of confabulation in more detail, special mention should be made of a particular category of brain injury which frequently gives rise to confabulatory disorders. Confabulation following rupture and repair of anterior

communicating artery (ACoA) aneurysms has been reported by several researchers (Alexander & Freedman, 1984; Burgess & McNeil, 1999; Damasio *et al*, 1985b; Delbecq-Derouesne *et al*, 1990; DeLuca, 1993; DeLuca & Cicerone, 1991; D'Esposito, Alexander, Fischer, MacGlinchy-Berroth & O'Connor, 1996; Downes & Mayes, 1995; Fischer, Alexander, D'Esposito & Otto, 1995; Gade, 1982; Irle, Wowra, Kunert, Hampl & Kunze, 1992; Johnson *et al*, 1997; Kapur & Coughlan, 1980; Laiacona, DeSantis, Barbarotto, Basso, Spagnoli & Capitani, 1989; Morris, Bowers, Chatterjee & Heilman, 1992; Moscovitch, 1989; Parkin *et al*, 1988; Vilkki, 1985; Volpe & Hirst, 1983, for a review see DeLuca & Diamond, 1995). Indeed it is common enough to have been described along with amnesia and personality change as a key feature of "anterior communicating artery syndrome" (Alexander & Freedman 1984; Damasio *et al*, 1985b, DeLuca & Diamond, 1995).

Ruptured aneurysms of the anterior communicating artery are associated with highly variable damage to the basal forebrain, basal ganglia and frontal association cortex. Although the primary features of the ACoA syndrome are confabulation, amnesia and personality change, several other features may be present. DeLuca & Diamond (1995) have highlighted the most frequent pattern of impairments. In general intelligence is relatively preserved, as are attention and concentration. Memory tends to be impaired, with particular deficits in anterograde memory. Performance on tests of immediate recall varies, but most patients' performance has been reported to be relatively intact. Delayed recall performance on the other hand tends to be significantly compromised, with an almost complete loss of information after a delay. Deficits in contextual and source memory have also been reported, in temporal memory (Parkin *et al*, 1988; Johnson *et al*, 1997; Eslinger & Damasio, 1984; Damasio *et al*, 1985b), spatial memory (Mayes, Meudell & McDonald, 1991) and in discriminating the modality of presentation (visual vs. auditory) (Shoqeirat, 1989, cited in DeLuca & Diamond, 1995). Oversensitivity to interference has also been reported. Implicit memory seems to remain intact. Executive performance generally seems to be impaired; there have been reports of poor performance on card sorting tasks, verbal fluency, and cognitive estimates. There is also evidence of a relationship between performance on executive tests and the extent of

retrieval difficulties (Simard, Rouleau, Brosseau, Laframboise & Bojanowsky, 2003). Visuo-spatial and perceptual abilities, and language functions appear relatively preserved. Whilst the classical syndrome of amnesia, confabulation and personality change is frequently referred to, DeLuca & Diamond (1995) note that relatively few patients present with all of these impairments.

1.2.5.1 The Critical Lesion Site for Amnesia in the ACoA Syndrome

Identifying the anatomical regions responsible for the amnesia observed in ACoA patients has presented a puzzle. The perforating branches of the ACoA supply the basal forebrain, the anterior cingulate, the anterior hypothalamus, the anterior columns of the fornix, the septal nuclei, the anterior comissure and the corpus callosum. Damage following ruptured aneurysms of the ACoA therefore tends to be restricted to the ventromedial frontal lobe, encompassing the orbitofrontal cortex and midline and paramedial basal forebrain. However the areas more traditionally associated with amnesia; the medial temporal lobes, diencephalon and thalamus, are intact.

There is some evidence linking the ventromedial frontal cortex to memory. For example Petrides (1989) notes that the posterior parts of the orbital and medial frontal lobe probably have close relationships with limbic structures in the mesial part of the temporal lobe. The ventromedial frontal cortex may therefore constitute a major component of a limbo-thalamic system underlying memory (Bachevalier & Mishkin, 1986). Mishkin (1982) has also proposed that lesions of the ventromedial frontal cortex, as it includes the projection sites of the medial temporal lobe limbic system structures, might cause a form of the organic amnesia syndrome.

There is now increasing evidence that the critical region for the memory impairments following ACoA aneurysms may be the basal forebrain. For example, Damasio *et al*, (1985b) reported five patients who had suffered basal forebrain damage. They noted a prominent amnesic syndrome and personality change in each one, and proposed that damage to the basal forebrain may be responsible. Amnesia in the ACoA syndrome may arise directly from damage to basal forebrain structures. However a further possibility is

that memory deficits arise due to malfunctioning in the hippocampal system, secondary to damage in the basal forebrain structures with which it is interconnected. The basal forebrain is a major source of the neurotransmitter acetylcholine, and is thought to contribute to memory function by providing cholinergic innervation to the hippocampus and amygdala, as well as to most of the neocortex. This hippocampal malfunctioning could therefore be caused by a reduction in neurotransmitter innervation. Volpe, Herscovitch & Raichle (1984), for example, have reported medial temporal lobe metabolic abnormality in two amnesic ACoA patients using PET, supporting the hypothesis that basal forebrain damage may lead to amnesia due to compromised medial temporal functioning.

The basal forebrain / acetylcholine hypothesis is supported by evidence suggesting that the cholinergic system is the primary neurochemical mediator of memory. There is now extensive evidence that cholinergic mechanisms modulate learning and memory (Easton & Parker, 2003; Gold, 2003; Thiel, 2003), possibly via mediation of attentional processes and allocation of attentional capacities (Sarter, Givens & Bruno, 2001; Sarter, Bruno & Givens, 2003). Destructive lesions of cholinergic neurons are associated with memory loss in both animals (Irle & Markowitsch, 1987) and humans, in Alzheimer's disease (Whitehouse, Price, Clarke, Coyle & DeLong, 1981), Korsakoff's syndrome (Butters, 1985) and Parkinson's disease (Whitehouse, Hedreen, White & Price, 1983). Scopolomine, a cholinergic antagonist, has also been shown to impair recall and lead to high levels of intrusions (e.g. Broks, Preston, Traub, Poppleton, Ward & Stahl, 1988). Hasselmo (1995) has also posited a critical role for acetylcholine in memory functioning, proposing that that it may be responsible for switching between a predominant influence of extrinsic stimulation (learning) and a predominant influence of intrinsic response (memory).

However Irle *et al* (1992) have argued that basal forebrain lesions alone are insufficient to result in amnesia. In an extensive study of 57 ACoA patients they found that neither basal forebrain nor striate lesions alone were sufficient to produce memory deficits. They argued that combined striate and basal forebrain lesions were necessary and sufficient to

produce amnesia, with additional ventromedial frontal lesions adding little to the deficit (see also Goldenberg, Schuri, Gromminger & Arnold, 1999, who propose that the nucleus accumbens, part of the ventral striatum, may be the critical site for basal forebrain amnesia). However striatal involvement has not been supported in a SPECT study by Rousseaux, Huglo & Steinling (1994). Therefore DeLuca & Diamond (1995) suggest that at present, the basal forebrain seems reliably implicated in amnesia as part of the ACoA syndrome, but that the roles of the striatum, gyrus rectus, anterior cingulate and basal ganglia, implicated in many reports, need to be further explored.

1.2.5.2 The Critical Lesion Site for Confabulation in the ACoA Syndrome

Identifying the critical lesion necessary for confabulation in the ACoA syndrome has also been difficult. However in most cases, confabulation has been attributed to frontal involvement. Vilkki (1985) reported five patients who had suffered rupture and repair of ACoA aneurysms resulting in severe memory disorders. However confabulation and false recognition were present in only two cases, both of whom were the only patients with established frontal lobe damage. Fischer *et al* (1995) in their study of 9 ACoA patients offered further evidence that the degree of confabulation is related to the extensiveness of frontal lesions. Five of their patients displayed spontaneous confabulation, severe anterograde amnesia, poor attentional and executive functions and denial of illness. All of these patients had multiple lesions involving the basal forebrain, ventral frontal lobe and striatum. The other four patients showed only momentary or provoked confabulation. The lesions in this group were restricted to the basal forebrain except for one patient who had additional orbitofrontal damage. They therefore concluded that extensive damage to both the medial basal forebrain and frontal systems was necessary to produce spontaneous confabulation with profound executive and memory deficits (see also Beeckmans, Vancoillie & Michiels, 1998). More limited lesions restricted to the basal forebrain or orbitofrontal cortex would lead to provoked confabulation and a more restricted pattern of deficits.

Most evidence has therefore suggested that basal forebrain and frontal damage in combination are necessary to produce confabulation (De Luca, 1993; De Luca &

Cicerone, 1991; De Luca & Diamond, 1995; Fischer *et al*, 1995; Vilkki, 1985). However, there is some evidence to suggest that confabulation may result from basal forebrain damage alone, in the absence of frontal pathology. Morris *et al* (1992) reported a patient (SJ) with persistent global anterograde and retrograde amnesia and confabulation with a small discrete lesion in the right diagonal band of Broca. SJ had suffered no damage to the ventromedial prefrontal cortex, so Morris *et al* (1992) concluded that frontal involvement could not be critical for confabulation to occur. However it should be noted that SJ's confabulation resolved over the 19 days following surgery, so is less severe than many other reports.

Hashimoto, Tanaka & Nakanbo (2000) have also reported a patient with an amnesic confabulatory syndrome (whose confabulation persisted for three months) with a discrete right basal forebrain lesion. They suggested that the septal nuclei and diagonal band of Broca might be the critical lesion sites for these difficulties, as they are the primary sources of cholinergic input to the hippocampus. However they note that their patient's lesion would also have disrupted the connections of the two limbic circuits important for memory: 1) the medial limbic circuit involving the medial temporal lobes, and 2) the lateral limbic circuit involving the anterior temporal cortex and amygdala, dorsomedial nucleus and orbitofrontal cortex.

It may be that milder forms of confabulation can arise from isolated basal forebrain damage, and that these patients displayed provoked and not spontaneous confabulation (cf. Fischer *et al*, 1995). However it is also possible that frontal dysfunction was also involved in the genesis of confabulation in the patients reported by Morris *et al* (1992) and Hashimoto *et al* (2000) via damage to the lateral limbic circuit involving the orbitofrontal cortex. In most cases it seems that involvement of both frontal and basal forebrain damage are implicated in confabulation.

1.3 THEORIES OF AUTOBIOGRAPHICAL MEMORY AND CONFABULATION

Theories seeking to account for the memory impairments seen following frontal lobe damage have several features to explain. We have seen that frontal damage may lead to occasional impairments in working memory and in prospective memory, deficient metamemory function, increased sensitivity to interference, impaired memory for the source and temporal order of information, deficits in free recall (and sometimes recognition) memory tests, pathological false recognition, intrusions, and occasionally confabulation. Most theories have been developed to explain the most dramatic of these symptoms, confabulation, and have grown out of the observations of earlier researchers on the possible frontal mechanisms underlying this phenomenon. These theories tend to fall into one of two categories: those that focus on temporal and source monitoring deficits, and those that focus on control of retrieval processes. Both of these types of account will be described in turn.

1.3.1 Source and Temporal Memory Deficit Theories

This category of theories has been prompted by evidence of the link between frontal lobe lesions and impaired memory for source and temporal information (Butters *et al*, 1994; Daum & Mayes, 2000; Janowsky *et al*, 1989b; Kesner *et al*, 1995; Kopelman *et al*, 1997b; Milner *et al*, 1985, 1991; Schacter, 1987; Schacter *et al*, 1984; Shimamura *et al*, 1990; Stanhope *et al*, 1998). Confabulation is seen as a consequence of a range of source or reality monitoring deficits that may result from impairments in encoding, retrieval, motivation or judgement processes. Can confabulation be explained as "source amnesia magnified and extended to include a lifetime of experience" (Moscovitch, 1989, p138)?

1.3.1.1 Johnson and Colleagues: The Source Monitoring Framework

The work of Johnson and colleagues on reality monitoring and source monitoring (e.g. Johnson & Raye, 1981; Johnson, Hashtroudi & Lindsay, 1993) provides a framework for investigating the processes involved in identifying the origins of information. They suggest that the subjective experience of remembering involves a rapid and unconscious

attribution process by which current mental events are attributed to particular sources on the basis of their qualitative characteristics, such as perceptual, contextual, and semantic information. Memories from different sources differ in characteristic ways that can, in principle, be used to identify the source of that information. For example perceived events will be associated with perceptual information (e.g. colour or sound), and with contextual (spatial and temporal) information, more semantic detail and more affective information. Imagined events, on the other hand tend to be associated with cognitive operations. Source monitoring is assumed to capitalise on these differences, therefore memories with perceptual and contextual detail will be judged as being externally derived, and will result in a recollective experience, whereas memories without such characteristics will be judged as being internally derived, and result in a feeling of familiarity with no conscious recollection.

Source monitoring involves two kinds of judgement processes: a) an evaluation of the qualitative characteristics of retrieved information (e.g. the type and amount of perceptual detail), and b) a more deliberative evaluation of retrieved information in the light of other supporting memories and knowledge, which checks for consistency, plausibility and coherence. These judgements are assumed to be dependent on processes that take place during encoding, when the features of complex memories are bound together, during the retention interval, when memories may be rehearsed or embellished, and at retrieval. Source monitoring processes may be disrupted when the availability of differentiated information regarding source is reduced, causing subjects to rely more heavily on undifferentiated global familiarity information in making their source judgements. The criteria by which information is evaluated may also vary from relatively stringent to lax, depending on the situation. In addition source monitoring judgements will be affected by the weighting of the characteristics associated with particular pieces of information, so that if semantic information is more salient than contextual or perceptual information, this may contribute most to the attribution of that memory to an internal or external source.

Johnson (1997) argues that there are a number of reasons to suspect that the frontal lobes are involved in source monitoring processes. Firstly, they are likely to be involved in circuits with the hippocampus to promote feature binding (Goldman-Rakic, Selemon, & Schwartz, 1984; Johnson, 1997; Shallice, Fletcher, Frith, Grasby, Frackowiak, & Dolan, 1994). Frontal regions are also believed to mediate several processes involved in strategic retrieval, including the maintenance of representations and evaluative processes (Baddeley & Wilson, 1986; 1988; Norman & Shallice, 1986; Stuss & Benson, 1986). Neuropsychological evidence from patients with frontal lesions also strongly suggests that damage to this area results in deficits in temporal order information, and source identification (see section 1.1.1).

This theory therefore explains false recognition and confabulation in terms of either unusually vivid mental experiences, which are later mistaken for real experiences, or the implementation of unusually lax criteria in distinguishing between real and imagined experiences. Vivid but plausible ideas may pass an initial reality monitoring check based on their qualitative characteristics, and be unchallenged by more systematic processes checking for consistency, plausibility and coherence. However if there is also disruption in these more systematic checking processes, possibly as a result of more extensive frontal damage, bizarre or fantastic confabulations could result.

Johnson (1997) describes a patient WL who, following a ruptured ACoA aneurysm, showed high rates of false recognition in a source monitoring task. She was shown words and pictures, and asked to create mental images for the words she saw. She was later given a recognition test in which she was shown a series of words that she had to identify either as items that she had previously seen, or new items. For items classified as "old", she was asked to say whether they had originally been presented to her as words or pictures. Shortly after rupture of her aneurysm WL falsely identified 12 out of 32 new items as old, and said that nearly all of these had been presented as pictures. One year later, however, she showed a normal pattern of performance. Johnson (1997) argues that her initial false recognition arose because she was using too simple a heuristic to make recognition judgements. If a picture came to mind, or the concept seemed familiar in

some way, she would accept the memory as a real event. This lax criterion was also used to explain her confabulation, which cleared by the second session along with her false recognition. A similar argument could also be used to explain the false recognition and confabulation displayed by BG (Curran *et al*, 1997; Schacter *et al* 1996) JB (Parkin *et al*, 1996, 1999), MR (Ward & Parkin, 2000), RW (Delbecq-Derouesne *et al*, 1990) and NH (Downes & Mayes, 1995).

However there are several lines of evidence that suggest the source monitoring account is not an adequate explanation for confabulation. Johnson *et al* (1997) compared a confabulating patient GS (who had suffered rupture of an ACoA aneurysm) with 3 normal controls and 3 non-confabulating patients with frontal damage. On a source monitoring task, both GS and the frontal control group showed a normal recognition hit rate (accurately identifying which of a list of words and sentences had previously been presented) but were impaired at correctly identifying which of two speakers had read them. Source monitoring ability alone did not therefore distinguish between a patient with confabulation, and those without. However GS did give less autobiographical information than the frontal control group on an autobiographical memory test, and gave more supporting details for imagined events that he incorrectly said he had participated in. Johnson *et al* (1997) concluded that confabulation may therefore be due to an interaction between a vivid imagination, an inability to retrieve autobiographical memories systematically, and source monitoring deficits, rather than to any one deficit alone. The source monitoring account has also come under criticism by investigators who point out that a deficit in memory verification processes cannot explain why more unusual confabulatory ideas are produced by subjects in the first place (e.g. Dab, Claes, Morais & Shallice, 1999; Dalla Barba 1993a).

Other theories concentrate more exclusively on the temporal memory deficit observed in frontal patients, attributing confabulation to disruption of a patients "temporal frame of reference" (Talland, 1965, p56). As early as 1932 Van der Holst postulated a fundamental "disturbance of time sense" leading to an inability to set experiences in a chronological frame as the mechanism of confabulation in Korsakoff's syndrome. In this type of theory

confabulating patients are hypothesised to be unable to sequence events temporally, so that events that are related but widely separated in time and place become fused or misattributed to another context.

1.3.1.2 Dalla Barba: Temporal Consciousness

Dalla Barba (1993a, b, 1995, 1999, 2001) has argued strongly against the source monitoring hypothesis, on the grounds that it does not explain why confabulations are most often seen in the episodic rather than semantic domain, and in some cases restricted exclusively to the episodic domain (patient MB, Dalla Barba, 1993a,b; patient GA, Dalla Barba, Capelletti, Signorini & Denes, 1997). If confabulation arises from an impairment in the monitoring processes that are used to decide whether information derives from perception or imagination, it should be present across all domains, and not limited to autobiographical or episodic retrieval.

Dalla Barba *et al* (1997) further tested the source monitoring hypothesis in a confabulating patient GA who had suffered sub-arachnoid haemorrhage following rupture of an ACoA aneurysm. On a source monitoring task in which she was required to identify whether she had previously been presented with an item in picture form, or asked to imagine it in picture form, she attributed 50% of her false recognition to the "seen" category, and 50% to the "imagined" category. Therefore Dalla Barba *et al* (1997) argued that her confabulation cannot have been due to a general bias to misconstrue imagined events as real, as she was equally likely to misidentify her false memories as imaginings. Furthermore, in a recognition test in which she was presented with a sample of real events, and events that she had confabulated, GA accepted more of the confabulatory than real events as genuine memories. Her confabulation therefore cannot be a result of simply accepting any autobiographical memory as real due to a faulty monitoring process, or she would not have rejected the real events as false. Similarly, patient PL (Dalla Barba, 1999) displayed a temporal gradient in her confabulation, with a high rate of confabulation for recent events where her veridical memory was worst, and a low rate of confabulation regarding remote events where her memory was intact. Dalla Barba

argues that the source monitoring account cannot explain why she would have been able to monitor remote memories but not more recent ones[1].

Dalla Barba (1993a) also argues against the hypothesis that confabulation arises due to a failure to "monitor out" inaccurate memories. Whilst he agrees that a monitoring failure has some role to play in confabulation, he comments that there must be some additional reason for incorrect memories to arise in the first place. His patient SD for example confabulated that he had been awarded a piece of meat on his right knee for winning a race, and it seems extremely unlikely that normal subjects have to routinely reject ideas such as this in their everyday recall. Instead Dalla Barba argues that confabulation will reflect the degree of memory impairment, with a deficit in semantic memory giving rise to more bizarre and fantastic examples of confabulation.

In his study of MB, Dalla Barba (1993a,b) noted that confabulations in the episodic domain tended to be accompanied by "remember" rather than "know" responses. MB's false memories seemed to be accompanied by the same recollective experience as true memories: he was "remembering 'another' past". However Dalla Barba argues that viewing confabulation as a disorder confined to long-term memory is too restrictive. Patient GA (Dalla Barba *et al*, 1997) also confabulated in questions relating to her orientation to time and place in the present, and to questions relating to her future. She was "remembering "another" past and planning "another" future". He therefore concludes that confabulation is not only a disturbance of memory but also of consciousness, and as such involves all subjectively experienced temporality: the personal past, present and future.

His theory carries several assumptions (Dalla Barba, 1999, 2001):

1) Events in the long term store are atemporal modifications.
2) These modifications can vary in stability (due, for example, to the number of times they have been retrieved).

[1] One reason for this may in fact have been that the rates of memory errors prior to monitoring in retrieval were greater for recent events rather than remote ones, where monitoring requirements were reduced.

3) There are different types of consciousness. Temporal Consciousness (TC) describes an awareness of something as a part of one's personal past and Knowing Consciousness (KC) describes being aware of something as a meaning or an element of impersonal knowledge or information.
4) TC is a more evolved form of consciousness, which is based on and dependent on KC.
5) As it is more evolved, TC uses less stable modifications of the long-term store in order to remember the past, be oriented in the present and project the future.

According to this model, episodic confabulation is caused by a condition in which TC is there but cannot make use of less stable modifications in the long-term store, only more stable ones. These patients are aware of their past, present and future but employ only the most stable elements from their long term memory stores in making temporal judgements. Therefore when asked what they will do tomorrow, or what they have done today, they will reply with the well-established routines or habits of a lifetime, however irrelevant they are to the current situation. Semantic confabulation, on the other hand would result from a condition in which KC is still there but is unable to use the more stable modifications of the long-term store. Finally, fantastic or bizarre confabulations in episodic memory, and semantic confabulation regarding word meanings can be explained by a condition where modifications in the long-term store are degraded so that the material used by TC and KC is incoherent[2].

1.3.1.3 Schnider and Colleagues: Temporal Context Confusion

Schnider and colleagues have recently developed another theory of confabulation based around the observation that confabulations often tend to be made up of elements of true events misplaced in time. Schnider von Daniken & Gutbrod (1996a) investigated 16 amnesic confabulating subjects of mixed aetiologies. They split the group into 6

[2] This concept of temporal consciousness is reminiscent of Wheeler, Stuss & Tulving's (1997) work on autonoetic consciousness (see also Tulving's work on chronesthesia, 2002). They argue that the frontal lobes underly this ability to mentally represent and become aware of subjective experiences in the past, present and future. Confabulation, they argue, is a disorder of autonoetic consciousness.

spontaneous confabulators and 11 provoked confabulators, with those who acted on their confabulations being defined as spontaneous confabulators, and those who produced intrusions on the California Verbal Learning Test being defined as provoked confabulators. Neither group's confabulation could be attributed to a deficit in storing new information, as both groups performed well on a continuous recognition task. Similarly they were able to exclude "gap-filling" as an explanation for their subjects' confabulation, as neither group differed from a control group in the degree to which they attempted to answer fake questions about non-existent items: neither group made up answers to conceal the gaps in their knowledge. They also found no consistent link between confabulation and performance on frontal executive tests: no consistent pattern of impairment was found in their patients, and the spontaneous confabulators did not differ from the provoked confabulators on any frontal measure.

However they did made a number of interesting observations regarding differences between the two groups. Firstly, the two types of confabulation were observed to doubly dissociate: some of the provoked confabulators did not spontaneously confabulate, and more interestingly, some of the spontaneous confabulators did not produce provoked confabulations (intrusions on the CVLT). Thus the two types of confabulation appeared to be qualitatively different disorders rather than more or less severe manifestations of the same disorder (in contrast to De Luca & Cicerone, 1993; Kapur & Coughlan, 1980; Shapiro *et al*, 1981). Secondly, the presence of either spontaneous or provoked confabulation was associated with different patterns of performance when the continuous recognition task was repeated one hour after the first run. In this second run the distractors from the first run were now used as the target items, and the previous targets were among the distractors. Thus subjects could not base their responding on the familiarity of the items, as they had seen them all before. Instead, they had to respond only to items that had appeared already in the present run. Spontaneous (but not provoked) confabulation was associated with "temporal context confusion" (TCC) - a relative increase in false positives in the second run compared to the first, with subjects falsely alarming to items that were previously targets, but which should now be ignored. Schnider *et al* (1996a) argued that spontaneous confabulation was associated with an

inability to recognise the temporal order of stored information that resulted in the erroneous recollection of memory elements that do not belong together. Provoked (but not spontaneous) confabulation, on the other hand, correlated with a number of measures of verbal learning and verbal fluency, and this type of confabulation was attributed to a wide search in a deficient memory, where intrusions were a trade off for an increased hit rate.

Schnider & Ptak (1999) set out to establish the origins of the temporal context confusion (TCC) associated with spontaneous confabulation. They theorised that TCC could arise from a) a failure to represent new information saliently enough to stop old information intruding into current thinking, or b) a failure to distinguish between representations of ongoing reality and previously acquired information, because spontaneous confabulators fail to suppress activated memory traces and mental associations in the face of current reality.

They used the same continuous recognition task for both meaningful and meaningless designs, only this time they had four runs. In each run the same set of stimuli were used, with different items selected as targets, and the rest serving as distractors. Subjects had to indicate only the items that reoccurred within each specific run, so after the first run they could not rely on familiarity information to make their responses. Schnider & Ptak (1999) reasoned that a failure to strongly represent incoming information would result in defective target detection with a low number of hits. However an inability to suppress previously acquired information, would result in the production of increasing numbers of false positives from run to run, with a normal hit rate.

18 amnesic subjects (6 spontaneous confabulators and 12 non-confabulators) and 10 normal controls took part in the experiment. Again, the groups did not differ on their performance on frontal executive tasks (verbal and nonverbal fluency and Stroop). Nor did they differ on the number of correctly identified targets, or "hits". However the spontaneous confabulator group differed from both other groups in their steep increase in the number of false positives from run to run. Their hits did not increase, so this was not

due to a bias to say "yes", or to an insufficiently broad search in memory. Instead these patients seemed to be failing to suppress mental associations that were not currently relevant.

It seems that in these patients, new incoming information provokes associations which remain active rather than being suppressed. "A chaos of memory traces, their associations, and new information which would have current behavioural relevance, thus guides thinking and behaviour" Schnider (2001, p157). This state can explain preserved or false recognition (in terms of a feeling of familiarity with many pieces of information) and impaired recall (as patients cannot normally access previously encountered information) as well as a lack of insight (as patients have no sense of a lack of information) and disorientation (as they cannot decide which pieces of information pertain to the present). Schnider (2001) argues that this deficit easily explains the pervasiveness of spontaneous confabulation, and does not require an additional deficit in monitoring processes following retrieval. Other forms of confabulation (by their definition, any confabulation which is not spontaneously acted upon by the patient) may result from different factors, for example an enhanced or impaired strategic search in memory.

In support of their theory, Schnider, Ptak, von Daniken & Remonda (2000a) have reported that temporal context confusion, and not performance on tests of memory or executive function, exactly paralleled the course of spontaneous confabulation in 8 spontaneous confabulators. Patients who recovered from spontaneous confabulation also recovered their ability to distinguish between currently relevant and previously encountered but currently irrelevant information, and to suppress these memory traces (as measured by their continuous recognition procedure). In fact, they have reported only one case of a spontaneous confabulator who did not show their temporal context confusion effect (Ptak & Schnider, 1999), but this patient appeared to be using an uncommonly stringent recognition criterion, and when motivated to improve his recognition performance did show a TCC effect. Schnider, von Daniken & Gutbrod (1996b) have also reported that orientation in 21 amnesic subjects was better predicted by this measure

of TCC than by the ability to acquire new information. And Schnider (2000) has reported preliminary evidence suggesting that spontaneous confabulators also have a problem in processing information in the very short-term range of the "now" – the duration of an experiential process.

Schnider & Ptak (1999) attributed the TCC effect to a loss of temporal labelling of stored information, which in all their patients was associated with lesions in the basal forebrain, medial hypothalamus or medial orbitofrontal cortex. These areas were not damaged in non-confabulating amnesics, who had posterior medial temporal and dorsolateral prefrontal lesions. They propose that the anterior limbic system (the loop connecting the amygdala, the dorsomedial nucleus and the orbitofrontal cortex) is critical for suppressing currently irrelevant mental associations of previously encountered info, and therefore for representing ongoing reality. Interestingly, they note that orbitofrontal lesions in animals also produce a failure to suppress previously established habits and responses that are no longer rewarded (Jones & Mishkin, 1972; Meunier, Bachevalier & Mishkin, 1997).

Schnider, Treyer & Buck (2000b) conducted a PET imaging study to test the hypothesis that orbitofrontal and basal forebrain structures are necessary for distinguishing between mental representations of ongoing reality and currently irrelevant memories. They used a similar continuous recognition design but with five runs separated by only 90 seconds. Brain activity was measured on the first, third and fifth runs. Their baseline task involved responding to immediate picture repetitions, and was designed to have virtually no memory component. Activation associated with this task was then subtracted from activation in the experimental task.

New learning on the first run was associated with strong, predominantly right hemisphere, medial temporal activation including the hippocampus, parahippocampal and fusiform gyri. Left parahippocampal gyrus activation was also observed, as well as a small area of activation in the right rectal gyrus. Consistent with the hypothesis that this reflected new learning, this activation decreased and was no longer detectable in the third and fifth runs.

In contrast, in the third and fifth runs, when the main requirement was to distinguish between item repetitions in the present run and previous presentations in earlier runs, activation of the posterior medial orbitofrontal cortex was observed. In the third run a large area of activation was observed in the posterior portion of the left inferior frontal gyrus, lateral of the rectal gyrus. In the fifth run this was smaller, and there was a new area of activation in the posterior medial orbitofrontal cortex (OFC) on both sides. The data hinted at a differential role for the left and right orbitofrontal cortex depending on familiarity with the task, or with the stimuli, but this difference was insignificant.

This pattern of activation seems to support their clinical data perfectly. Posterior medial OFC and basal forebrain lesions (or lesions to areas with connections to these anterior limbic structures, see Ptak, Birtoli, Imboden, Hauser, Weis & Schnider, 2001) appear to be critical in sorting out mental associations pertaining to ongoing reality by suppressing memory traces that have no current relevance. The exact mechanisms by which this occurs are not clear, but it appears to represent more than simple response inhibition, as imaging of a task investigating inhibition of responses to just seen but currently false items activated the lateral prefrontal cortex but not the orbitofrontal cortex (Jonides, Smith, Marshuetz, Koeppe & Reuter-Lorenz, 1998). More anterior lesions may have secondary effects in this posterior medial OFC region, for example by compressing it, but on the basis of imaging evidence do not seem to be critical themselves.

In a further study exploring *how* the OFC may mediate neocortical activity and deactivate memories that are not currently relevant, Treyer, Buck & Schnider (2003) replicated these findings with four different stimuli types, and further found that this selection process was associated with activation of subcortical structures contiguous with left OFC activation and involving the left caudate nucleus (ventral striatum, head and body of the caudate), the left substantia nigra and ventral tegmental area, and the right medial thalamus. These structures are part of a frontal subcortical loop connecting the OFC with itself and the prefrontal neocortex and are modulated by dopaminergic structures.

Schnider (2001) proposes that in the healthy brain, associations that do not pertain to current reality are suppressed or deactivated even before they reach consciousness. Thus "before the content of an evoked memory is recognised, it has already been checked and adjusted according to whether it relates to ongoing reality or not". In support of this he reports an ERP study in which healthy subjects completed a continuous recognition task similar to that used with their patients. They found that correct suppression of distracters in run two of the task was associated with distinct alteration of cortical activity after 220-300 ms, characterised by the absence of a specific cortical potential map configuration and continued positivity of a frontal potential, rather than the negative deflection characterising all other stimulus responses. Thus the processing of currently irrelevant memories seemed to induce suppression of a processing stage rather than an additional cortical process, and this alteration was presumed to be the cortical expression of an anterior limbic suppression mechanism that actually occurs even earlier. Learning and recognition, on the other hand, was characterised by cortical amplitude modulation after 400-480 ms (Schnider, Valenza, Morand & Michel, 2002).

The results from these experiments are indeed striking. However it is not entirely clear how this suppression of memory traces that are currently irrelevant might occur. A major problem for theories positing a fundamental temporal deficit as the mechanism underlying confabulation has been the existence of patients with disordered temporality who do not confabulate. However Schnider and colleagues stress the differences between their task and more traditional tests of disordered temporality in frontal patients. Traditional tasks they say, for example those that require subjects to identify which of two lists a word came from, do not distinguish between confabulators and non-confabulating amnesics in the same way that their repeated continuous recognition task does (Schacter, 1987; Milner *et al*, 1991; Shimamura *et al*, 1991; Kesner *et al*, 1995; Johnson *et al*, 1997). Failure on those tasks is typically associated with lateral prefrontal cortex damage, which never alone produces failure on the Schnider task, which appears to critically involve anterior limbic structures rather than the dorsolateral prefrontal cortex. They also yield different patterns of activation in imaging tasks, activating the lateral prefrontal cortex but not the orbitofrontal cortex (Zorilla, Aguirre, Zarahn, Cannon

& D'Esposito, 1996; Cabeza, Mangels, Nyberg, Habib, Houle, McIntosh & Tulving, 1997b). Therefore they argue that these tasks may be tapping different processes, although exactly what these differences are is unclear.

However temporal context confusion, as with the source monitoring explanation, can only be a partial explanation for confabulation, as it fails to explain a) the existence of confabulations that are selective in content and stable over time (e.g. Burgess & McNeil, 1999), and b) the existence of fantastic and bizarre confabulations. These beliefs would seem to require more explanation than simply failing to suppress irrelevant associations. Similarly Kopelman et al (1997a) noted that whilst many (especially episodic) confabulations may result from conflation and inappropriate retrieval of "real" memory fragments out of temporal sequence, others (especially semantic confabulations) often seem to result from perseverations or from the patient giving instantaneous ill-considered and unchecked responses to immediate environmental and social cues.

1.3.2 Retrieval Process Theories

The shortcomings of source and temporal memory based theories of confabulation mean that many researchers have preferred to adopt theories that attribute confabulation to a deficit in the control of retrieval processes. Many of these theories are based on theories of normal episodic retrieval, and may include and build on many of the elements of the theories discussed so far, rather than competing with them. They are an extension of dysexecutive accounts of confabulation, but tend to be more explicitly concerned with deficits in memory retrieval processes than general cognitive control processes. Whilst encoding deficits have been implicated in some aspects of the memory deficits involved in frontal lobe damage (e.g. Incisa della Rochetta, 1986), most theories concentrate on impairments at the retrieval stage rather than at encoding, consolidation or storage, as a result of the observation that confabulation tends to occur as much in recall of remote, pre-traumatic events as it does in post-traumatic ones (but see Dalla Barba, 1999). These theories view the frontal lobe as the neural substrate underlying the organisation of a search in long-term memory, and evaluating the results of this search, and hypothesise that confabulation results from a failure in these processes.

1.3.2.1 Moscovitch: Strategic Retrieval

Moscovitch (1989, 1992, 1995; Moscovitch & Melo, 1997) argues that the temporal memory deficit theory is not sufficient to account for confabulation. Although a temporal memory deficit is a prominent feature of confabulation, he characterises it as a symptom not a cause. A temporal memory deficit cannot account for spontaneous, fantastic confabulations, neither can it account for confabulation in the semantic domain. Furthermore Moscovitch & Melo (1997) in their analysis of the content of confabulations, found a greater number of content than temporal errors. Similarly Moscovitch argues that accounts that place the deficit at the monitoring stage, after memory has been retrieved but before a response is emitted, don't account for the evidence that early retrieval processes involved in memory search are also impaired. Patients cannot retrieve answers to some questions that should be readily apparent, implying an additional deficit in retrieval strategy.

Moscovitch therefore distinguishes between strategic, and associative or cue-dependent retrieval processes. Associative or cue-dependent retrieval involves relatively automatic processes that are engaged when a specific proximal cue interacts with information stored in memory. The material retrieved in response to this cue is either the target memory, or provides material for subsequent strategic retrieval processes. Strategic retrieval involves self-initiated, goal-directed, effortful, intelligent processes that are initiated when associative retrieval cues have proved inadequate. A search is then organized using whatever knowledge is available to reinstate the appropriate context and locate the cue that allows local associative processes to operate. Once a memory trace is recovered, other strategic processes then monitor the output, determining whether it satisfies the goals of the memory search, and whether it is consistent with other information in semantic and episodic memory. Strategic retrieval processes are therefore "problem solving routines applied to memory" (Moscovitch, 1995, p234).

In order for confabulation to occur, Moscovitch argues that three conditions must apply:

1) There must be faulty output from the associative / cue-dependent retrieval system. This will result in retrieval errors in normal subjects, and especially if memory is impaired.
2) Strategic search processes must also be impaired, resulting in the production of misleading cues and inappropriate memories, and exacerbating the problem of faulty output. Impairments in these strategic processes account for errors of omission, which would occur when cues are inadequate and do not trigger responses, and also for the benefit of external prompting and cues, which would enable a strategic search to be initiated, but also increase the risk of confabulation (Moscovitch & Melo, 1997).
3) Monitoring processes must also be defective, meaning that the resulting memory errors are not edited out. This stage accounts for the fact that a failure in stages 1 and 2 above in normal subjects will usually be corrected. Whilst the first two conditions are necessary for confabulation to occur, they are not sufficient to produce it without an additional monitoring deficit.

This theory applies equally to episodic and semantic memory, and to recent and remote memories. So why is confabulation more common in episodic than semantic memory, and why is temporal confusion such a prominent feature? Moscovitch argues that in Dalla Barba's (1993a) confabulation battery, semantic memory items made fewer demands on strategic retrieval than the episodic items. He also suggests that episodic retrieval in real life is likely to make more demands on the strategic retrieval system, leading to greater confabulation in this domain. He hypothesised that if the strategic demands in both episodic and semantic items were matched, confabulation would occur equally in both domains, and has reported evidence in support of this conclusion (Moscovitch & Melo, 1997, but see Dalla Barba *et al*, 1997). However, Moscovitch has also conceded that damage to memory systems will exacerbate confabulation and may be a prerequisite for it to occur. As the episodic memory system is more frequently impaired, this may affect the greater incidence of confabulation seen in this domain, possible as a result of the proximity of basal forebrain areas believed to be involved in episodic memory retrieval and ventromedial areas which he postulates may underlie strategic retrieval. Structures

associated with semantic retrieval (the inferior and lateral temporal lobes and lateral prefrontal cortex, see section1.4.1.1) are more remote and therefore may be less likely to be damaged in conjunction with the ventromedial prefrontal cortex (Moscovitch & Melo, 1997). In order to explain why temporal disturbance of memory seems to be such a prominent feature of confabulation, Moscovitch proposes that temporal organisation may be particularly sensitive to disturbances in strategic retrieval processes. He argues that memories are not stored or retrieved in chronological sequence (but see Dalla Barba *et al*, 1997, patient NL). Instead strategic retrieval processes are used to estimate the dates and order of retrieved events by relating them to known landmarks (Friedman, 1993).

Moscovitch's theory is consistent with neuroimaging evidence that as recovery of information becomes more practiced and automatic, and presumably therefore more reliant on associative / cue-dependent strategies than strategic ones, activation of the frontal lobes is diminished (Cabeza, Kapur, Craik, McIntosh, Houle & Tulving, 1997a; Nyberg, Cabeza & Tulving, 1996a; Nyberg, Tulving, Habib, Nilsson, Kapur, Houle, Cabeza & McIntosh, 1995). He argues that search processes are probably mediated by the lateral frontal cortex, and post-ecphoric monitoring and verification by the ventromedial frontal cortex, with the right side playing a more prominent role in both cases. This is consistent with evidence suggesting that the right frontal cortex is associated with confabulation and a tendency to make high numbers of false alarms (Burgess *et al*, 1996; Curran *et al*, 1997; Delbecq-Derouesne *et al*, 1990; Parkin, Dunn, Lee, O'Hara & Nussbaum, 1993; Schacter *et al*, 1996), and that it is involved in recollection in PET studies (e.g. Tulving, Kapur, Craik, Moscovitch & Houle, 1994 see section 1.4.1.2). He suggests that ventromedial frontal damage, possibly on the right, may be necessary, if not sufficient, to produce confabulation.

Moscovitch's strategic retrieval theory is relatively dependent on confabulating patients performing poorly on tests of free recall but within the normal range on tests of recognition, which would be less dependent on strategic retrieval processes. This is the most common pattern of performance observed (Kapur & Coughlan, 1980; Moscovitch, 1989; Parkin *et al*, 1988). However some patients have shown the reverse pattern, with

preserved recall and impaired recognition (e.g. patient RW, Delbecq-Derouesne *et al*, 1990). Moscovitch (1995) argues that different aspects of strategic retrieval may be impaired in this patient. If strategic processes are split into initial search and later post-ecphoric monitoring, RW must have had relatively preserved initial search processes allowing free recall, but faulty monitoring leading to a high false positive rate. Possibly more problematic for Moscovitch's theory are cases of confabulating patients who perform normally on frontal tasks that would intuitively seem to rely on intact strategic retrieval processes, for example the cognitive estimates test (Dalla Barba *et al*, 1997).

1.3.2.2 Burgess & Shallice: Descriptors, Editors and Mediators

A similar retrieval deficit theory has been proposed by Burgess & Shallice (1996), building on Norman & Shallice's (1986) characterisation of the frontal lobes as an supervisory attentional system (SAS) involved in governing complex non-automatic aspects of behaviour. Shallice (1988) proposed that the SAS may have two roles in memory, in setting up descriptions allowing access to specific events in memory, and in verifying the retrieved memories. According to this framework, frontal damage would result in memory problems due either to poor formulation and implementation of descriptions, or an impairment of verification systems.

Burgess & Shallice (1996) expanded on this theory by deriving a model of control processes in autobiographical memory retrieval from analysis of normal subjects autobiographical recall of everyday events. They propose that four types of processes are involved in episodic memory retrieval, operating on the long-term store. All but the first are memory control processes and are thought to be part of the supervisory system.

1) **Input templates**. These are pared down representations of a particular pattern of activation in the long-term store. They are not semantic memories, but are whole or partial generic memories rather than specific episodes, derived from perceptual and cognitive input and pre-existing (semantic) associations.

The activation of one of these input templates is "starting value" for recall, and subsequent narrowing down and respecification are then the domain of the modulatory system, made up of three memory control processes:

2) **Descriptor processes**. These produce a specification of the type of trace that would satisfy the demands of the retrieval task.
3) **Memory editor processes** are then continuously involved in checking that the output of the long-term store fits with previously retrieved elements, and with the overall task requirements. These editor processes are automatically triggered by the setting up of a description.
4) **Mediator processes**. If a possible contradiction is detected by the editor, cognitive (strategic and problem-solving) operations are put into operation. These also concern the adequacy or plausibility of retrieved elements but differ from editor processes in that they are under strategic control and are not limited to the mnestic domain. As such they are deliberate problem solving routines that address inconsistencies. They may then lead to memory respecification, i.e. the inputting of new descriptions, and the activation of new input templates to resolve contradictions.

Burgess & Shallice (1996) note that an impairment of the editor processes alone would explain Mercer *et al*'s (1977) finding of poor self correction in confabulators. However it does not explain why confabulating patients come up with so many erroneous memories in the first place. There must therefore be an additional source of error in confabulators' memory. An impairment at the level of the descriptor processes would account for this in that specification would be too noisy. Too wide an area of the long-term store would be activated, and inhibition of inappropriate parts of the space would be less strong. This would then increase the chances of inappropriate representations being produced as candidate memories, and of the conflation of different memory experiences.

If confabulators are unable to self-restrict their memory search, descriptors would at best reflect the external request made. This would explain the benefit of cueing in recall tasks

as in this case a description is explicitly provided. Intrusions from memories that have recently been primed or activated by input templates would also be explained as a result of extreme impairment of the descriptor processes resulting in stimulus-driven recall. Burgess & Shallice (1996) offer the example of patient LE, who confabulated that he had met with Harold Wilson after having completed a test of recognition of famous faces which contained a number of former prime ministers (Shallice, Burgess, Schon & Baxter, 1989).

Confabulators must therefore have damage to both description formation and editor processes[3]. In cases of bizarre and fantastic confabulations, Burgess & Shallice (1996) argue that there must also be damage to the mediator systems, resulting in poor plausibility judgements, hypothesis testing and reasoning. They argue that this type of impairment would explain why some confabulations become fixed and stable over time, as schematisation would occur after repeated strengthening of inappropriate associations, and recall would then be possible without the use of a description. Burgess & McNeil (1999) for example described a patient, BE, who displayed a single, stable confabulation that he had appointments to carry out stocktakes, and would attempt to leave the house each day to do this. The selectivity of his confabulation may be explained by the fact that stocktakes had been a frequent occurrence for him before his illness, and had thus become a generic representation, somewhere between an episodic and a semantic memory, and therefore an input template. Faulty monitoring processes meant that he could not reject this idea as inaccurate, so the chances of this idea recurring increased through schematisation, and the selectivity and stability of his false belief increased over time. Burgess & Shallice (1996) also account for the greater occurrence of confabulation in episodic memory by arguing that the control processes in their model are primarily involved in autobiographical rather than semantic memory. However confabulation may also occur in semantic memory as the long-term store accessed by description processes contains both episodic and semantic information.

[3] Although confabulation has been reported in association with an isolated descriptor impairment (Dab *et al*, 1999), and with an isolated editor impairment (Delbecq-Derouesne *et al*, 1990).

Burgess & Shallice (1996) summarise their model as follows. Descriptor processes produce a specification of the type of trace that would satisfy the demands of a retrieval task. Noisy specification will increase the chance of inappropriate representations being produced as candidate memories. Editor processes check that the output of the long-term store fits with previously retrieved memory elements and with the overall task requirements. An impairment at this stage may lead to responding to a question without adequate consideration, checking or self-correcting. Finally mediator processes control cognitive operations concerning the adequacy or plausibility of retrieved memory elements under strategic control. An impairment here would result in reasoning errors and bizarre or fantastic responses. As descriptor, editor and mediator processes are hypothesised to be part of the supervisory system (Norman & Shallice, 1986) they should be frontally controlled. Burgess & Shallice (1996) suggest that editor processes relating to verification are likely to be right frontal, description processes probably left frontal, and mediator processes bilateral (see section 1.4 for relevant evidence from neuroimaging)

1.3.2.3 Schacter, Norman and Colleagues: The Constructive Memory Framework

Norman & Schacter (1996) have argued against theories that make a distinction between strategic retrieval and monitoring processes (Moscovitch, 1989; 1995; Moscovitch & Melo, 1997), or description and verification systems (Burgess & Shallice, 1996), on the grounds that the information underpinning description or retrieval processes must necessarily be the same as that underpinning monitoring or verification. Both are derived from a representation of the event, and depend critically on the ability to reinstate the context associated with a particular episode. Instead they argued that all patients with frontal damage suffer from the same core deficit: an inability to retrieve contextual information pertaining to the sought-after episode.

An effective retrieval cue should overlap maximally with the sought-after trace and minimally with competing traces in terms of contextual features. Norman & Schacter (1996) proposed that phenomena such as false recognition, retrieval deficits and confabulation could be explained either by a partial breakdown in context retrieval

processes, resulting in a poorly focused representation of the context that would uniquely specify the sought-after episode, or a complete breakdown, leading to a total inability to generate a representation of the contextual features that define an event, and disrupting the retrieval and evaluation of stored information[4].

Schacter *et al* (1998) recently expanded their theory into the "constructive memory framework" (CMF) which, in contrast to the two theories discussed so far, emphasises the role of encoding operations as well as retrieval processes. They propose that memory errors may result from a) episodes which are not stored in a manner which allows them to be separately accessed at retrieval, b) retrieval cues that are not specific (focused) enough, or c) criterion-setting that is too lax.

In the CMF, representations of new experiences are conceptualised as patterns of features, with different features representing different facets of the experience. These are distributed widely across different parts of the brain, so that no single location contains a complete record of the trace of an experience. Retrieval of a past experience involves a process of pattern completion in which a subset of these features is activated and activation then spreads to the rest of the constituent features.

In order for retrieval to work effectively, the system must accomplish several tasks:
At encoding, these can be characterised as:

1) **Feature binding.** The features comprising an event memory must be linked together at encoding to form a coherent representation. If this does not occur source memory failure will occur when fragments are recalled without any recollection of how or when they were acquired. Source memory errors may also occur when binding processes are unimpaired but not enough information that is diagnostic of the source of the experience is included in a representation.

[4] Norman & Schacter (1996) note that their focusing concept is similar to Shimamura's (1995, 2000, 2002) idea of frontal memory impairments arising from an inability to inhibit irrelevant information. Damage to these mechanisms would result in too wide a focus. However their approach differs from Shimamura's in that inhibition is a by-product of activation and maintenance of a description of the sought-after episode.

2) **Pattern separation.** Bound episodes must then be kept separate in memory. If episodes overlap extensively we may recall the general similarities or gist of a group of experiences, but not the item-specific information required to distinguish one episode from another.

At retrieval, these can be characterised as:

1) **Focusing of retrieval search.** If retrieval cues match more than one episode there is an increased chance of recollecting information that is not relevant to the target episode, or of impaired recall of an episode's details due to interference from information from other episodes
2) **Pattern completion.** In response to a retrieval cue, a subset of the features comprising a particular episode are activated, and activation then spreads to the rest of the features associated with that episode.
3) **Criterion setting.** When the pattern completion process produces a match, the rememberer must decide whether the retrieved episode is the sought-after episode, and whether it is an episodic memory rather than an image, fantasy or thought. This source or reality monitoring process involves a criterion setting process in which the rememberer considers perceptual, semantic and other information in order to reach a decision (Johnson *et al*, 1993). A lax source monitoring criterion will increase the chances of accepting internally generated information as a memory of a real event.

Schacter *et al* (1998) use the CMF to explain the phenomena of false recognition, and intrusions and confabulations. False recognition, they argue, may be explained either by a failure of pattern separation at encoding, by a poorly focussed retrieval search, or by an implicit associative response which is not adequately monitored at retrieval. A failure of pattern separation may arise if there is unacceptably high overlap between item representations, for example when lists of semantically related items have been studied. Multiple representations will then be assigned to the same hippocampal index, which will lead to excellent memory for gist, but impaired recall of item-specific information. Similarly if the retrieval search is not focused enough, multiple episodes will be accessed and there will be poor memory for source specifying details, with retained memory for

gist. The resulting reliance on gist information will lead to false recall and recognition. Alternatively an implicit associative response may arise, e.g. if a related word is generated at the time of study in response to a presented word. Then false recognition could result from a source monitoring error if subjects failed to recollect whether they were actually presented with the item, or generated it internally. The CMF may therefore be able to account for the false recognition shown by RW (Delbecq-Derouesne *et al*, 1990), JB (Parkin *et al*, 1996, 1999), MR (Ward & Parkin, 2000) and BG (Curran *et al*, 1997; Schacter *et al*, 1996). BG, for example made many false alarms that were accompanied by "remember" rather than "know" responses. Schacter *et al* (1998) argue that this may be explained by the adoption of an inappropriate decision criterion at test, in which BG would respond "remember" if a test item matched the general characteristics of study items. This could stem either from an encoding deficit with a failure to encode item-specific information at study, or a retrieval deficit caused by an inability to form an appropriately focused description of the study episode, or an impairment in accurate source monitoring processes.

Intrusion errors in free recall and confabulations may also be explained in terms of the CMF. Both types of error may result either from a failure to construct a retrieval cue that is fully consistent with retrieved information, or from a source monitoring error which allows internally generated information to be accepted as a real event. In the first case, recall distortion may occur if, in the focusing phase, schematic knowledge and information present in the test environment is used to construct retrieval cues instead of more specific representations. Retrieved information may then be in keeping with the norm rather than reality. For example in a word list learning task semantically consistent but incorrect information may be retrieved. In confabulation, usual patterns of behaviour rather than current reality may be produced. Alternatively, source monitoring errors may fail to distinguish between associations that were produced during test and actually presented items, leading to false recall in structured test situations. They may also be responsible for a failure to monitor out imagined events in confabulation, especially if these imaginations are associated with increased perceptual or other contextual information, or if retrieval has been made more fluent by repeated imagining or retrieval.

The CMF may therefore explain the high intrusion rates shown by JB (Parkin *et al*, 1996, 1999) and RW (Delbecq-Derouesne *et al*, 1990) in recall tasks, as well as confabulation.

Schacter *et al* (1998) suggest that many brain areas are likely to be involved in these processes. Medial temporal areas are assumed to be involved in encoding, with the hippocampus implementing feature binding and pattern separation, and the neocortex later consolidating these memories (McClelland, McNaughton & O'Reilly, 1995). Medial temporal regions may also play a role in pattern completion at retrieval, either through the hippocampus for recent episodes, or directly between features in the neocortex for consolidated episodes. The role of the prefrontal cortex in their theory is less well defined. However the right PFC is suggested to be involved in the more effortful aspects of retrieval related to focusing of the memory search or to post-retrieval monitoring or criterion setting, on the basis of imaging studies (see section 1.4.1.2). The basal forebrain, as a major source of the neurotransmitter acetylcholine, is also implicated in regulating the dynamics of pattern completion processes in the hippocampus and other brain structures (Hasselmo, 1995).

Only three of the main retrieval process theories have been described here, but many other authors have offered similar accounts, some also extending them to include an important role for the "self" in influencing the content of confabulatory ideas and accounting for individual differences (Conway & Tacchi, 1996; Fotopolou *et al*, 2004; Kopelman, 1999). Retrieval theories incorporate a sufficiently wide range of mechanisms and processes to be able to account for many of the memory impairments associated with frontal lobe damage. Most explicitly address the reasons for confabulation, false recognition and intrusions, and they have been successful in explaining the concurrent amnesia displayed by most confabulators, and in exploring the spontaneous vs. provoked, and episodic vs semantic distinctions. Many also account for the higher incidence of recall impairments compared to recognition impairments, and some offer accounts of normal autobiographical memory, and the errors that may arise in the absence of brain injury. Certain aspects of these accounts have also proven useful in rehabilitation, for example Burgess & McNeil (1999) found that using a diary to cue recall helped their

patient BE to verify what he had been doing and prevented him from acting on his recurrent false beliefs. Similarly, Dayus & van den Brouke (2000) successfully used self-monitoring training to treat confabulation in patient WF (previously described by Downes & Mayes, 1995). They have therefore in general proved the most popular explanations of confabulation.

1.4. IMAGING STUDIES OF THE FRONTAL LOBES AND MEMORY

Over the last decade neuroimaging techniques, including event related potentials (ERP), positron emission tomography (PET), and more recently functional magnetic resonance imaging (fMRI) and event related fMRI, have begun to offer insights about the brain areas involved in memory processing in normal subjects. Convergent with the patient findings, imaging studies of memory almost always show activation of the prefrontal cortex (see Fletcher & Henson, 2001; Yancey & Phelps, 2001 for reviews). However in contrast to neuropsychological patient findings (where lesions are highly variable between subjects and often cover wide regions of the frontal lobes), imaging studies are able to provide more detailed clues to the anatomical specificity of frontal contributions to memory processing.

1.4.1 The HERA Model

One of the most significant contributions of neuroimaging work has been the development of the Hemispheric Encoding / Retrieval Asymmetry (HERA) model of memory. This theory arose from a series of studies that reported greater left than right frontal activation associated with encoding tasks, and greater right than left frontal activation associated with retrieval tasks (Kapur, Craik, Tulving, Wilson, Houle & Brown, 1994; Shallice *et al*, 1994; Tulving *et al*, 1994; see Nyberg *et al*, 1996a for a review).

1.4.1.1 Encoding

Episodic encoding has been found to consistently result in greater activation in the left

prefrontal cortex, and this activation tends to centre on the left ventrolateral prefrontal cortex, and in particular the inferior frontal gyrus. Kapur *et al* (1994) for example, reported that deep encoding was associated with increased activation in anterior and posterior left VLPFC. This pattern has been reported with both verbal material (Fletcher, Frith, Grasby, Shallice, Frackowiak & Dolan, 1995; Gabrieli, Desmond, Demb, Wagner, Stone, Vaidya & Glover, 1996; Shallice *et al*, 1994), and with non-verbal material (Grady, McIntosh, Rajah & Craik, 1998; Haxby, Ungerleider, Horwitz, Maisog, Rapaport & Grady, 1996). Nyberg *et al* (1996a) in their review found that 18 out of 21 comparisons investigating activation at encoding reported greater left PFC activation for more effective encoding tasks compared to less effective encoding tasks, and this was found in both incidental and intentional encoding tasks.

This left prefrontal activation has most often been associated with the retrieval of information from semantic memory which enables successful episodic encoding, in "deep" encoding tasks involving semantic processing compared to "shallow" encoding tasks which focus on surface features of the stimulus. Wig, Miller, Kingstone & Kelley (2004) for example reported that activation of the inferior frontal gyrus was sensitive to depth of encoding. Deep encoding activity is also more likely to lead to subsequent successful retrieval. Thus Henson, Rugg, Shallice, Josephs & Dolan (1999a) reported that words later recalled with a "remember" rather than a "know" judgement were associated with greater activity at study in the left posterior middle frontal gyrus and the ventral region of the left inferior frontal gyrus. They therefore attributed this left PFC activation to semantic elaborative processes that aid memory encoding. Activity in the left inferior frontal gyrus that is sensitive to the depth of encoding operations and predicts subsequent remembering has also been reported by Baker, Sanders, Maccotta & Buckner (2001) and Wagner, Schacter, Rotte, Koutsaal, Maril, Dale, Rosen & Buckner (1998c).

Activation of left PFC in association with semantic processing at encoding has therefore been widely demonstrated. However there is disagreement about what the specific role of the left PFC in semantic processing might be. Four hypotheses have been proposed.

1) Retrieval From Semantic Memory

Firstly, it may be that the left PFC is responsible for the simple generation or retrieval from semantic memory of semantic attributes and associates of the to-be-remembered material (e.g. Tulving *et al*, 1994). This position is supported by evidence that greater activation in the left PFC is associated with verb generation tasks than with simple verb reading tasks (Frith, Friston, Liddle & Frackowiak, 1991; Klein, Milner, Zatorre, Meyer & Evans, 1995; Petersen, Fox, Posner, Mintun & Raichle, 1988; Raichle, Fiez, Videen, Macleod, Pardo, Fox & Peterson, 1994). Semantic judgements are also associated with left PFC activation (Craik, Moroz, Moscovitch, Stuss, Winocur, Tulving & Kapur, 1999; Desmond, Sum, Wagner, Demb, Shear, Glover, Gabrieli & Morell, 1995; Wagner, Desmond, Demb, Glover & Gabrieli, 1997). Demb, Desmond, Wagner, Vaidya, Glover & Gabrieli (1995) also demonstrated that the left PFC was more active in deep than in shallow encoding, but was not affected by task difficulty, implying that it played a role simply in the retrieval of semantic information at encoding.

2) Maintenance Of Semantic Attributes In Working Memory.

An alternative explanation is that the left PFC is responsible not for the retrieval of semantic information, but for the maintenance of this information in semantic working memory during processing. Evidence in support of this proposal has been provided by Gabrieli, Poldrack & Wagner (1998) who compared two types of word-stem completion task; one group of stems had many completion options, whilst the other had very few. They reported greater left dorsolateral PFC activation for the stems with many completion options, and argued that this reflected the increased amount of semantic material to be maintained in semantic working memory.

3) Selection Of Semantic Attributes From Competing Alternatives.

Thompson-Schill and colleagues (Thompson-Schill, D'Esposito, Aguirre & Farah, 1997; Thompson-Schill, D'Esposito & Kan, 1999) have proposed a slightly different explanation for the activation of the left inferior frontal gyrus (IFG) in semantic retrieval tasks. Thompson-Schill *et al* (1997) examined performance of three semantic tasks: generation of a verb that was related to a visually presented noun, classification of a

stimulus, and comparison of two or more stimuli. In each case they created two versions of the task; a "Low Selection" condition where there was an obvious dominant response or where all semantic information was appropriate, and a "High Selection" condition where subjects needed to select an appropriate response from many competing pieces of semantic information. They found increased left IFG activation in the high selection versions of each task, and argued that activation of the left IFG is the result not of semantic retrieval *per se* but of the need to select some relevant feature of semantic knowledge from a set of competing alternatives.

Thompson-Schill *et al* (1999) asked subjects to generate colours or actions that were appropriate to cue words. Each cue word was presented twice, and subjects had to either generate the same type of response that they had generated the first time (colour-colour), or to generate the different response (colour-action). They found that the high competition condition (generating a different response) was associated with greater left posterior ventrolateral PFC activation and attributed this again to the increased selection demands in this condition.

This "selection" account has received some support from other studies. For example Dolan & Fletcher (1997) found greater left dorsolateral PFC activation when subjects were required to encode word pairings that emphasised a different semantic relationship to the relationship that they had encoded previously. Fletcher, Shallice & Dolan (2000) also found greater left ventrolateral PFC activation associated with new word pairings and for distantly related word pairings. Both studies highlight a role for the left PFC in selecting appropriate associations and suppressing inappropriate semantic associations of the study material, and are related to Nathaniel-James and Frith's (2002) notion of the left PFC being involved in "sculpting the response space", or selecting an appropriate set of responses for the task at hand.

4) Organisation Of Material At Encoding.

One final suggestion is that the left PFC is selectively involved in organising material at encoding on the basis of semantic relations or attributes. Fletcher, Shallice & Dolan

(1998a) asked subjects to memorise lists of 16 words in which the words were drawn from four semantic categories. The lists were either presented a) blocked by semantic category with the category names provided, b) randomly intermixed but with the category names provided, or c) randomly intermixed with no category names provided. They found that the greatest left dorsolateral PFC activation was associated with the last condition which placed the highest demands on subjective organisation at encoding. This activation was also found to decrease if the task was carried out with a concurrent distracting task which reduced organisation and subsequent memory performance. They attributed this left dorsolateral PFC activation to deriving the commonalities of meaning among the words in order to create an organisational structure.

Savage, Deckersbach, Heckers, Wagner, Schacter, Alpert, Fischman & Rauch (2001) have proposed a similar role for the left dorsolateral PFC. They compared spontaneous semantic organisation at encoding (where words from four categories were presented randomly), directed semantic organisation (where the same list presentation was used but subjects were explicitly directed to mentally group words together), and encoding of unrelated lists, and found that semantic clustering was associated with activity in the left inferior frontal gyrus and the left dorsolateral PFC. They concluded that these regions were involved in semantic organisation, monitoring and updating processes during encoding.

Wagner, Maril, Bjork & Schacter (2001) compared a task in which subjects had to maintain three words over a delay to one in which they had to reorder the words along a dimension (e.g. pleasantness). They reported that whilst both tasks were associated with left ventrolateral PFC activity, only the reordering task was associated with additional left dorsolateral PFC activity. This is similar to Fletcher *et al* (1998a) who also failed to activate the ventrolateral PFC in their study. Although the findings are not clear cut, one possibility is that whilst the left ventrolateral PFC (and specifically the inferior frontal gyrus) is critical for semantic processing at encoding, the left dorsolateral PFC may be specifically responsible for higher level control mechanisms involved in updating and manipulating representations, including organisation at encoding.

1.4.1.2 Retrieval

In contrast to studies of encoding, studies of episodic memory retrieval tend to report right sided prefrontal activation (see Rugg & Wilding, 2000 for a review). This activation tends to be centred upon the right anterior (area 10) and dorsolateral (areas 46 and 9) PFC (e.g. Tulving *et al*, 1994). Nyberg *et al* (1996a) in their review reported that 28 out of 32 comparisons involving subtraction of semantic retrieval from episodic retrieval tasks showed preferential right prefrontal cortex involvement. This appears to be consistent across a wide variety of tasks including recognition (e.g. Tulving *et al*, 1994), cued recall using word stems (e.g. Buckner, Petersen, Ojemann, Miezin, Squire & Raichle, 1995) category cues (e.g. Fletcher *et al*, 1995) and paired associates (e.g. Shallice *et al*, 1994), and across tasks using both verbal (e.g. Cabeza *et al*, 1997a; Kapur, Craik, Jones, Brown, Houle & Tulving, 1995; Nyberg *et al*, 1995) and non-verbal (e.g. Haxby *et al*, 1996; Moscovitch, Kohler & Houle, 1995; Tulving, Markowitsch, Craik, Habib & Houle, 1996) materials.

As with encoding several proposals have been made regarding the specific role of the right lateral PFC in retrieval operations.

1) Retrieval Success

One proposal is that the right PFC activation associated with retrieval tasks reflects ecphory – the reactivation of memory traces (Tulving, 1983). Thus this activation should only be seen when retrieval is successful. There is some evidence that right PFC activation is dependent on retrieval success from both ERP (Wilding & Rugg, 1996; Donaldson & Rugg, 1998; Duzel, Yonelinas, Mangun, Heinze & Tulving, 1997) PET (Rugg, Fletcher, Frith, Frackowiak & Dolan, 1996) and fMRI (Rugg, Fletcher, Chua, & Dolan, 1999; Saykin, Johnson, Flashman, McAllister, Sparling, Darcey, Moritz, Guerin, Weaver & Mamourian, 1999) studies. Greater right anterior PFC activation has also been reported during recognition of words previously studied deeply rather than shallowly (Buckner, Koutstaal, Schacter, Wagner & Rosen, 1998), and during recognition accompanied by "Remember" judgements (Henson *et al*, 1999a) which is consistent with

the retrieval success position. However several studies have reported right PFC activation when a retrieval attempt is unsuccessful (see below), or have argued that whether activation can be linked to retrieval success depends upon the task and the strategy adopted by subjects (e.g. Wagner, Desmond, Glover & Gabrieli, 1998a). Most authors now concur that the retrieval success concept may not be as useful as once thought (at least with regard to the prefrontal cortex), and alternative proposals for the role of the right PFC at retrieval have been sought.

2) Retrieval "Mode" / Retrieval "Attempt"

Recent evidence suggests that activation of the right PFC at retrieval is more likely to reflect a general retrieval attempt, or the creation and maintenance of an episodic retrieval "mode" (Tulving, 1983) rather than successful retrieval or ecphory, as the right PFC is more active than the left PFC when participants try to recognize presented test items, whether they succeed or not (Nyberg *et al*, 1996a). It also seems unaffected by retrieval difficulty (Nyberg *et al*, 1995), the form of the test (recognition or cued recall, Cabeza *et al*, 1997a) or the properties of the stimulus materials (verbal or non-verbal, Tulving *et al*, 1994). Nyberg *et al* (1995) for example found that all retrieval tasks (of deeply encoded, shallowly encoded, or non-presented words) activated the right prefrontal region compared to a reading baseline task, indicating that this reflected a general attempt to recognize stimuli. Similarly Kapur *et al* (1995) and Duzel, Cabeza, Picton, Yonelinas, Scheich, Heinze & Tulving (1999) reported equivalent levels of right frontal activation in recognition tasks with low and high densities of old words. Rugg, Fletcher, Frith, Frackowiak & Dolan (1997) reported greater right dorsolateral PFC activation in intentional compared to incidental recognition tasks, also indicating that this reflected the adoption of a retrieval mode.

Wagner *et al* (1998a) also reported similar activation across varying levels of retrieval success and retrieval effort so argued that their results supported a retrieval attempt hypothesis, which more specifically they said would reflect the initiation of a retrieval search or the evaluation of the products of retrieval. They argued that right frontal activation can depend upon the context of the retrieval attempt and on the task

instructions, which change the retrieval strategy adopted by participants. For example in blocks where many items are new and there are few targets, subjects may adopt a strategy of relying purely on familiarity with little organized search or evaluation of the products of a memory search. By contrast in blocks where many items are old they may be more likely to engage in search and evaluative retrieval processes during each recognition attempt. This strategy adoption account may explain some previously contradictory results, in that task context and even the degree of retrieval success that subjects experience within a trial may influence their retrieval strategy. (See Johnson, Nolde, Mather, Kounios, Schacter & Curran, 1997, for similar arguments about the effects of blocking).

Lepage, Ghaffar, Nyberg & Tulving (2000) in their meta-analysis tried to identify retrieval mode or "REMO" sites which were critical for retrieval attempt not success, and found six sites all in the frontal lobes. Five were within the PFC, three strong ones in the right hemisphere (in the frontal pole, BA 10; the frontal operculum, BA 47/45; and a lateral dorsal area BA8/9), two weaker sites in the left hemisphere (again in the frontal pole and operculum), and one in the medial anterior cingulate. They concluded that their results supported the HERA model, and the concept of a general retrieval mode. However there is also the intriguing possibility that there may be functional dissociations between these regions.

3) Retrieval Effort

A slightly different proposal to the concept of a general retrieval mode is the idea that right prefrontal activation may reflect retrieval *effort* in more difficult retrieval situations. Schacter, Alpert, Savage, Rauch & Albert (1996a) gave their participants a word stem cued recall task for words that had previously been studied either deeply or shallowly. They found greater anterior frontal (BA 10) activity for those words that had been shallowly encoded than for those that had been deeply encoded, and concluded that this activation reflected the greater retrieval effort required in this condition[5]. Similar results

[5] It should be noted that the activation Schacter *et al* (1996a) found was primarily left frontal rather than right. This contradiction to the HERA model is discussed further below.

have been reported by Rugg *et al* (1997) who found greater anterior frontal activation during recognition of words that had been studied shallowly, implying that this region was specifically recruited when traces are weak or words are difficult to retrieve.

4) Post-Retrieval Monitoring

An alternative account of the right prefrontal activation associated with retrieval is that it reflects post-retrieval processes such as monitoring and checking of the products of a memory search (e.g. Gabrieli 1998, Shallice, 2001). ERP studies have provided evidence of a late onsetting right frontal positivity in recognition tasks that seems to follow ecphory, and has been attributed to post-retrieval monitoring (see Allan, Wilding & Rugg 1998 for a review). Curran, Schacter, Johnson & Spinks (2001) for example reported a late frontal old-new effect in their false memory paradigm, but only amongst those participants who were good at discriminating between true targets and lures. They argued that this reflected the use of effective evaluation and monitoring processes which enabled true memories to be distinguished from distractors. This monitoring explanation may also explain why old – new difference effects (which had been presented as evidence for retrieval success accounts of right PFC activation) are found in recognition tasks but not in cued recall tasks. Monitoring is likely to be equal for old and new items in cued recall, but will only occur in recognition after successful recognition (Allan, Wolf, Rosenthal & Rugg, 2001).

Fletcher, Shallice, Frith, Frackowiak & Dolan (1996) in a PET study of retrieval of word pairs found that bilateral dorsolateral PFC and anterior PFC activations decreased as the semantic relatedness between cue and response decreased. But right anterior PFC activation then increased again from weakly related to completely random pairs. They argued that this U-shaped pattern of activation reflected post-retrieval monitoring. Strongly related word pairs are assumed to require checking to ensure that that it is a true memory and not just an associative response that is being produced, more weakly related pairs need less checking as they are more distinctive, but pairs with no relation at all require more checking again to ensure that the right pairing is being made.

Several other studies have found support for the monitoring hypothesis. Fletcher, Shallice, Frith, Frackowiak & Dolan (1998b) compared internally cued recall (free recall cued only by the word "next", so organised by the subject) with externally cued recall (cued by a category name which fitted only one word from the previously presented list). They found greater right dorsolateral PFC activation in the internally cued condition than in the externally cued condition and attributed this to the greater monitoring demands involved in keeping track of your performance in free recall. In contrast they found greater posterior ventrolateral PFC activation in the externally cued than in the internally cued condition, which was attributed to a cue specification process.

Henson, Shallice & Dolan (1999b) compared an inclusion condition (in which subjects had to respond "yes" to previously presented words) to two exclusion conditions (in which subjects had to respond "yes" to previously presented words only if they were also presented in either the same spatial position or the same temporal position as their initial presentation). They found greater bilateral dorsolateral PFC activation for both of the exclusion conditions, and attributed to this to the extra checking stage which was required in these conditions compared to the inclusion condition. The results of Henson *et al* (1999a) are also consistent with this hypothesis, as they found greater right dorsolateral activation associated with items that were given a "Know" response rather than a "Remember" response. Items which are familiar in the absence of recollection are likely to require more checking and monitoring to ensure that the products of the retrieval search are sufficient for the task. Similarly Henson, Rugg, Shallice & Dolan (2000) found more right dorsolateral PFC activation for items recognised with low confidence than for items recognised with high confidence, again presumably reflecting the greater checking that was required for low confidence items[6].

This right dorsolateral involvement in post-retrieval checking and monitoring processes has received support from several other sources. It is consistent with evidence that the mid-dorsolateral frontal cortex (areas 46/9) is involved in keeping track of actions and

[6] It should be noted that the retrieval effort and monitoring hypotheses are in fact closely related, as checking processes will necessarily require more effort than simple familiarity judgements.

expected events so as not to repeat them (Petrides, 1994; Petrides, Alivisatos, Evans & Meyer, 1993a; Petrides, Alisivatoss, Meyer & Evans, 1993b). It is also consistent with neuropsychological studies reporting that patients with right frontal lesions produce abnormally high numbers of repetitions in their recall (Stuss *et al*, 1994), may produce pathologically high levels of false alarms (BG, Curran *et al*, 1997; RW, Delbecq-Derouesne *et al*, 1990) and are impaired at metamemory judgements (Kopelman, Stanhope & Guinan, 1998a; Schnyer *et al*, 2004; Vilkki *et al*, 1998). Finally it has received support from two studies using rTMS evidence, which found that stimulation of the right dorsolateral PFC during retrieval led to high error (false positive) rates (Rossi, Cappa, Babiloni, Pasqualetti, Miniussi, Carducci, Babiloni & Rossini, 2001; Sandrini, Cappa, Rossi, Rossini & Miniussi, 2003).

1.4.2 Source Monitoring

Henson *et al*'s (1999b) inclusion/exclusion study raises the possibility that one component of the monitoring process may be source monitoring, for example monitoring of the temporal and spatial context associated with retrieved memories to ensure that they meet the demands of the retrieval situation. Some evidence in support of this hypothesis has been reported. For example Schacter, Reiman, Curran, Sheng Yun, Bandy, McDermott & Roediger (1996b) reported activation of the right anterior PFC (area 10) and orbitofrontal cortex (area 11) in association with false recognition but not true recognition in a PET study, and similar right anterior PFC activity was reported in a subsequent fMRI study (Schacter, Buckner, Koutstaal, Dale & Rosen, 1997). The late onset of this activity implies an involvement in processes acting on the output of the memory system and involved in error detection, and Johnson (1997) has argued that this is consistent with involvement in source monitoring processes. Johnson, Kounios & Nolde (1996) have also reported that frontal sites are in general more associated with source monitoring activities than simple yes /no recognition.

However most studies that have specifically compared retrieval of source as opposed to item recognition have activated the left rather than the right prefrontal cortex. For

example Nyberg, McIntosh, Cabeza, Habib, Houle & Tulving (1996b) reported that whilst retrieval of item memory activated the right inferior PFC, retrieval of source information regarding the spatial presentation of the item activated the left middle frontal gyrus, and retrieval of temporal information about presentation activated the anterior cingulate. Greater left PFC activity has also been reported in source memory tasks compared to item recognition tasks in areas 46, 44, 10 and 9 (Nolde, Johnson & D'Esposito, 1998a) and in BA 10, 45 and 47 (Fan, Snodgrass & Bilder, 2003). Similarly Ranganath, Johnson & D'Esposito (2000) reported greater activation of the left anterior middle frontal gyrus (BA 10/46) in recalling perceptual information about the presentation of a target (whether the object provided as a retrieval cue was bigger or smaller than the originally encoded picture) compared to simple old/new recognition. Rugg *et al* (1999) also found greater left anterior PFC activation (specifically left BA 10, and the left inferior frontal gyrus and opercular cortices BA 45/47) in a spatial source retrieval task. Cansino, Manquet, Dolan & Rugg (2002) reported that correct source memory for spatial information was associated with activation in the left middle frontal gyrus (BA 10/32), more medially, in addition to the left superior frontal gyrus (BA 9). And Dobbins, Foley, Schacter & Wagner (2002) found that source memory was associated with greater activation in left lateral frontal regions including the ventrolateral and posterior dorsolateral PFC, the frontopolar PFC, and the medial aspect of the superior PFC.

In interpreting the functional significance of this activation Ranganath *et al* (2000) have argued that this left PFC activation reflects monitoring or evaluative processes that are engaged when you try to retrieve information from memory. Dobbins *et al* (2002) have proposed an even more specific model in which the anterior ventral extent of the left inferior PFC, due to it's links with semantic processing, is responsible for cue specification for retrieval processes, whilst the left posterior dorsolateral and frontopolar regions reflect monitoring and verification of the products of memory retrieval.

However this left PFC activation is not consistent with the HERA model which would predict *right* PFC activation in retrieval tasks. In fact some studies have found both left

and right activation associated with retrieval of source. For example Henson *et al* (1999b) reported right and left dorsolateral activation in the middle frontal gyrus associated with retrieval of source information. Whether it was spatial or temporal information did not make any difference to activations. They argued that the right dorsolateral activation reflected monitoring processes, and the left activation might reflect either deep verbal elaboration at retrieval resulting in further encoding, or may subserve monitoring too. In the study by Henson *et al* (1999a) anterior frontal activation was specifically associated with "Remember" rather than "Know" responses, so they proposed that this activation reflected successful retrieval of source information. Slotnick, Moo, Segal & Hart (2003) also found bilateral PFC activations in the left and right middle frontal gyri, the left and right and medial superior frontal gyri and the left inferior frontal gyri associated with retrieval of spatial source information. Indeeed Cabeza, Locantore & Anderson's (2003) production monitoring hypothesis (discussed below) would predict bilateral PFC activation in source memory tasks in the left ventrolateral PFC (subserving semantic generation and production of retrieval cues) and the right dorsolateral PFC (subserving checking and monitoring processes), and they found this pattern of activation in their source recognition task, along with an additional right frontopolar region.

1.4.3 Developments since the HERA model

Evidence linking left prefrontal activation to the retrieval of source information has posed a problem for the HERA model, which has linked left prefrontal activations to encoding and right prefrontal activations to retrieval processes. In fact several other studies have also reported results in contrast to these predictions. Involvement of the right PFC has been reported at encoding (Henson *et al*, 1999b; Henson *et al*, 2000; Ranganath *et al*, 2000; Rugg *et al*, 1997; Sandrini *et al*, 2003; Schacter *et al*, 1997). Some authors have argued that lateralisation reflects the type of material to be encoded rather than the nature of the processing, with visual material activating the right rather than the left PFC (Brewer, Zhao, Desmond, Glover & Gabrieli, 1998; Golby, Poldrack, Brewer, Spencer, Desmond, Aron & Gabrieli, 2001; Kelley, Miezin, McDermott, Buckner, Raichle, Cohen, Ollinger & Petersen, 1998; Lee, Robbins, Pickard & Owen, 2000; Lee, Robbins, Smith,

Calvert, Tracey, Matthews & Owen, 2002; Wagner, Poldrack, Eldridge, Desmond, Glover & Gabrieli, 1998b). Baker *et al* (2001) have proposed that an additional right hemisphere region in the precentral gyrus may be involved in specifically in non-semantic encoding processes, for example in shallow encoding tasks.

Activation of the left PFC has also been reported in retrieval tasks (Buckner *et al* 1995, 1998; Kapur *et al*, 1995; Lee *et al*, 2000, 2002; Rugg *et al*, 1997; Schacter *et al*, 1996a; 1997; Tulving *et al*, 1994, 1996). This activation has generally been attributed to additional semantic retrieval engaged during the memory test to further encode stimuli (e.g. Nyberg *et al*, 1996a; Buckner, Wheeler & Sheridan, 2001), however Nolde, Johnson & Raye (1998b) have proposed a rather different explanation (see discussion below).

It should be remembered that the HERA model was initially developed as a model of *verbal* encoding and retrieval, so it is not surprising that the use of visual materials has an effect. Secondly it claimed only that there was a greater left than right involvement at encoding, and a greater right than left involvement at retrieval. It did not claim that the left PFC would have no involvement at retrieval nor that the right PFC would have no involvement at encoding, so it is not surprising that some bilateral activations are reported, especially given that different comparison procedures are used in different studies. Perhaps most critically it did not make any detailed specification of how different areas within the right and left PFC may be functionally distinct, and this is the area in which the most valuable developments to the model have been made. For example it has been proposed that whilst more posterior areas of the PFC may be affected by the type of material to be encoded or retrieved, more anterior regions may reflect control processes that are not lateralised according to modality (Buckner, 2003; McDermott, Buckner, Petersen, Kelley & Sanders, 1999; Wig *et al*, 2004; Yancey & Phelps, 2001). In addition several converging sources of information have indicated that the ventrolateral PFC may be particularly sensitive to novelty and that this information may be useful for making recognition judgements (Buckner *et al*, 1998; Kopelman, Stevens, Foli & Grasby, 1998b; Knight & Nakada, 1998; Tulving *et al*, 1996; Yonelinas, Kroll, Dobbins, Lazarra & Knight, 1998).

Recent theories have proposed that rather than distinguishing areas according to the type of material being processed, or according to whether encoding or retrieval processes are being carried out, the regions of the PFC that are activated depend on the type of task or the type of processing that is being conducted. For example, two recent theories have specifically addressed the bilateral activity or left lateralised activity often seen in retrieval tasks.

Nolde *et al* (1998b) in their review of the literature noted that whilst relatively simple retrieval tasks reveal right lateralised activity, more demanding retrieval tasks tend to reveal left lateralised or bilateral activity in the dorsolateral and anterior PFC. They argue that the right dorsolateral and anterior PFC subserve relatively simple reflective or "heuristic" processes involved in the temporary maintenance and comparison of information, for example refreshing activations, shifting between representations and noting relations. The left dorsolateral and anterior PFC is additionally recruited for more complex episodic retrieval tasks which involve more complex reflective or "systematic" processes involved in the more detailed analysis of information, maintaining information during analysis and self-cueing to retrieve additional information, for example rehearsing, and initiating and generating cues for retrieval.

This "CARA" (cortical asymmetry of reflective activity) hypothesis explains the left PFC activity seen in source monitoring tasks, and the fact that bilateral or left PFC activation is more often seen in more complex cued recall and free recall tasks in comparison to simple recognition tasks (as such it also explains the left activation attributed to retrieval effort by Schacter *et al*, 1996a). In these tasks subjects have to retrieve and evaluate additional episodic detail and develop and maintain criteria for evaluating traces. More simple tasks on the other hand will show activity restricted to the right PFC.

Cabeza *et al* (2003) have proposed a slightly different account in their "Production Monitoring Hypothesis". They argue that the left PFC is involved in semantically guided information production assumed to be more involved in recall (in generating cues), and the right PFC is more involved in monitoring and verification processes assumed to be

involved in recognition tasks (in rejecting distractors). This activity is assumed to be independent of retrieval effort or retrieval success. This theory receives some support from ERP evidence suggesting a progression from early left to later right lateralised processes in retrieval (e.g. Allan *et al*, 1998). Differing amounts of production and monitoring activity will be required in different types of recall and recognition tasks. For example they argue that more production will be required in associative recognition and context recognition tasks than in simple item recognition tasks, hence the differences observed in activity.

Cabeza *et al* (2003) used this reasoning to explicitly test their theory against Nolde *et al*'s (1998) CARA model. They conducted a PET study comparing activity in four types of retrieval task: stem cued recall, associative cued recall, context (source) recognition, and item recognition. They argued that their model would predict more production (left lateralised) processing in stem cued recall and associative cued recall, and more monitoring (right lateralised) processing in context recognition and item recognition. Nolde *et al*'s (1998) CARA model on the other hand would predict more systematic (left lateralised) processing in stem-cued recall and context recognition, and more heuristic (right lateralised) processing in associative cued recall and item recognition tasks. In keeping with the predictions of the Production Monitoring Hypothesis they found that the left ventrolateral PFC (BA 45) and the anterior cingulate (BA 32) were more active for the recall tasks, whilst the right dorsolateral PFC (BA 46/44) and anterior PFC (BA 10) were more active for the recognition tasks. On the basis of these results they argue that semantic processes are subserved by the left ventrolateral PFC, and manipulation processes involved in monitoring are subserved by the right dorsolateral PFC. Within the right PFC they argue that some areas may be involved in general monitoring (e.g. BA 9/44 and 46/10), whilst others may be more specific to context retrieval (e.g. the dorsal right PFC region, and the right frontopolar region). This reasoning would predict that the right dorsolateral region would be critical in false recognition, as damage to this area would allow semantically guided processing (e.g. of semantically related lures) to go unchecked, and therefore also receives some support from neuropsychological evidence.

Other theorists do not specify laterality in their theories at all, but concentrate on functional dissociations of the ventrolateral, dorsolateral and anterior PFC. One view of this distinction has been that the dorsolateral PFC is involved in the temporary storage and maintenance in working memory of spatial information and that the ventrolateral PFC is involved in the temporary storage and maintenance of object information (Goldman-Rakic, 1988). However the evidence in support of this hypothesis is at best patchy (see D'Esposito & Postle, 2002) and most accounts now take a process-specific rather than a domain-specific view. Petrides (1994, 1995) proposed that the ventrolateral PFC is where organisation of information received from posterior association areas is performed, whereas the dorsolateral PFC was additionally recruited only when monitoring and manipulation of information was required. This view has received rather more support than Goldman-Rakic's (D'Esposito & Postle, 2002; Owen, 1997), and similarities to it can be seen in many more recent theories combining evidence from working memory and episodic memory.

Fletcher & Henson (2001) reviewed imaging studies of working memory and episodic memory and concluded that certain general supervisory processes were critical to both (see also Nyberg, Forkstam, Petersson, Cabeza & Ingvar, 2002; Nyberg, Marklund, Persson, Cabeza, Forkstam, Petersson, Ingvar, 2003, and Ranganath, Johnson & D'Esposito, 2003, for evidence that some processes involved in working memory, episodic memory and semantic memory may be shared). Fletcher & Henson (2001) concluded from their review that the ventrolateral FC is involved in updating and maintaining the contents or working memory. This can take the form of rehearsal (in working memory), generation of semantic attributes (in episodic encoding), or cue specification (in episodic retrieval). The dorsolateral FC on the other hand is involved in selecting, manipulating, and monitoring the contents of working memory. This may take the form of manipulation (in working memory), organisation of material, or selection amongst semantic attributes (in episodic encoding) or monitoring (in episodic retrieval). Finally the anterior FC is involved in the higher order functions of selecting processes, goals and subgoals (see also Rugg, Fletcher, Allan, Frith, Frackowiak & Dolan, 1998),

and metamemory processes (e.g. evaluating performance and reviewing strategies)[7]. (See Petrides, 2002, for similar proposals regarding the ventrolateral role in active strategic retrieval and the dorsolateral involvement in monitoring processes).

Moscovitch & Winocur (2002) have proposed a similar account to that of Fletcher & Henson (2001). They too argue that the ventrolateral PFC (specifically area 47) is involved in cue specification and/or maintenance at encoding or retrieval. In support of this they cite studies indicating that ventrolateral PFC is activated in recognition regardless of the number of items held in memory or of the complexity of the operations, so appears to be involved in specifying the information that needs to be recovered (e.g. Henson *et al*, 2000; Wagner, 1999). They also cite evidence indicating that the ventrolateral PFC is involved in encoding information distinctively (Brewer *et al*, 1998; Wagner *et al*, 1998c). A failure in either of these mechanisms can lead to over-reliance on gist and subsequent memory errors (left at encoding, or right at retrieval), and these failures would also account for poor recall. The mid-dorsolateral PFC (specifically areas 9/46), on the other hand is proposed to be responsible for the monitoring and manipulation of information held in working memory. In support of this they cite studies indicating that the dorsolateral PFC is activated in studies involving increased complexity of operations (e.g. Duncan & Owen, 2000; Christoff & Gabrieli, 2000; Petrides, 1995, 2000; Postle & D'Esposito, 2000), and in studies requiring monitoring operations (Fletcher *et al*, 1998b; Henson *et al*, 2000).

Their theory differs from Fletcher & Henson (2001) in positing a role for the ventromedial frontal cortex (BA areas 11, 13, 25 and possibly 32) in what they term automatic "feel-rightness" for anomoly or rejection, based on basic rejection criteria in terms of goals and cues. A failure in this process would lead people to accept strong recovered memories as veridical even if they were false, and could lead to confabulation. BA 10, they argue, is responsible for "feel-rightness" for acceptance or endorsement in cases of uncertainty, based on strategic retrieval of contextual information. Finally BA 6

[7] Alternatively, Christoff & Gabrieli (2000) have proposed that the anterior PFC may be specialised for the monitoring of internally generated information.

is posited as the critical site for response selection among competing alternatives (i.e. in selecting among events and details in memory).

In summary then Moscovitch & Winocur's (2002) model states that the dorsolateral PFC formulates a strategy for retrieval, the ventrolateral PFC specifies the retrieval cues, and information is then retrieved from the hippocampal complex. This information then goes through two stages of possible rejection in the ventromedial PFC and the frontal pole, with monitoring and evaluation processes overseen by the dorsolateral PFC. Finally response selection is undertaken by BA 6.

1.4.4 The Medial and Orbital Frontal Lobe and the Basal Forebrain

In most of the studies and theories mentioned so far attention has been concentrated on the lateral PFC, and findings relating to the medial and orbitofrontal frontal lobe have been scarce. One reason for this is that these regions are difficult to image with fMRI. For example, many studies have been insensitive to orbitofrontal activity because of signal loss caused by susceptibility artefact. However some findings are now beginning to emerge.

The orbitofrontal PFC has extensive interconnections with medial and anterior temporal and retrosplenial cortical regions thought to be essential for memory formation, so it probably plays an important role in memory processing. Frey & Petrides (2002, 2003) for example have reported right orbitofrontal activation associated with increased encoding demands for abstract visual information and for visually presented faces. They argue for a key role for areas 11 and 25 in encoding processes, and say the orbitofrontal cortex is likely to be part of a mnemonic circuit rather than representing a general executive function. Savage *et al* (2001) have also argued that the ventromedial PFC, and especially the orbitofrontal cortex, is implicated in strategy mobilization. They reported that activity in this region predicted which subjects would later spontaneously exhibit effective semantic strategies in their task measuring organisation at encoding. They argue that the ventromedial PFC mobilises strategies which are then undertaken by the left PFC at encoding.

The ventromedial frontal lobe, particularly on the right, is also argued to be critically involved when subjects reflect on their own mental states (Frith & Frith, 1999; Stuss & Levine, 2002), and this is supported by the patient findings of Schnyer *et al* (2004) who reported that impairments in feeling-of-knowing were particularly associated with damage to the right ventromedial cortex. The medial frontal cortex has also been associated with the retrieval of autobiographical event memories as opposed to memory retrieval *per se* (Graham, Lee, Brett & Patterson, 2003; Maguire, 2001), indicating a possible role in monitoring information relating to the self and internal mental states.

Fujii, Okuda, Tsukiura, Ohtake, Miura, Fukatssu, Suzuki, Kawashima, Itoh, Fukuda & Yamadori (2002) have recently reported the first successful detection of basal forebrain activity in a functional imaging study. Their task involved cued recall of previously memorised words either from temporal cues (subjects were asked to recall words memorised either the day before the scan, or the morning of scan) or from person cues (whether the word had been presented by a man or a woman). They found that recall from temporal cues was associated with activity in the basal forebrain, the right middle frontal gyrus (and posterior sites), whilst recall from person cues was associated only with the right middle frontal gyrus (and posterior sites). Percentage increases of regional blood flow in the basal forebrain correlated with successful recall. On the basis of these results they argued that the basal forebrain plays a critical role in successful episodic memory recall, especially in time contextual information[8].

Although more evidence is required, the association of these diverse functions with the medial and orbitofrontal PFC and the basal forebrain is intriguing given that spontaneous confabulation also tends to occur after damage to these regions. The fact that confabulation seems to involve failures in autobiographical memory, monitoring of internal states, and temporal processing indicates that further studies of these regions is likely to be fruitful.

[8] There has also been some evidence for involvement of the medial PFC in temporal memory in rat work (e.g. Mitchell & Laiacona, 1998), and temporal memory has been associated with acetylcholine function in the frontal cortex (Meck, 1996).

1.5 AIMS OF THE THESIS

The frontal lobes account for approximately one third of the human brain. However researchers have until recently only infrequently mentioned specific regions of the frontal lobes in relation to memory. In neuropsychological studies lesions in all areas of the frontal lobes have often been grouped together. However lesions in different areas of the PFC may produce different patterns of impairment. Imaging studies have started to offer clues to the fractionation of the frontal lobes, implying that there is functional specialisation of the PFC, and that different subregions implement different functions relevant to episodic memory. Now a combination of these approaches is necessary.

A combination of lesion and neuroimaging studies is likely to be powerful in informing theorizing on memory systems. Such an approach may go some way towards controlling for the drawbacks of each approach individually. Imaging studies tell us which regions are involved in a particular task, but not whether these regions are critical. A demonstration that inactivation of a region disrupts the function in question is necessary before we can infer from imaging evidence that a particular brain region is necessary for a particular function. This is where lesion studies come in. This combination of imaging and lesion studies is an important new direction for neuroscience, and Ranganath & Knight (2003) and Shallice (2003), amongst others, have recently commented on how findings from the two areas might be linked.

As we have seen, imaging studies have reported a variety of regions of the lateral prefrontal cortex to be involved in memory control processes relating to encoding and retrieval. However most neuropsychological studies thus far have not been thorough enough to lend support to or to conflict with these theories. For example it is unclear why there appears to be a different pattern of recall and recognition impairments in lesion studies, when both task show a similar pattern of activation in imaging studies (Cabeza *et al*, 1997a). Although perfect concordance should not be expected, the relationship between these two sources of evidence needs to be explored.

To date, only two studies have been conducted which explicitly address the links between imaging and lesion studies. Swick & Knight (1996) in one of the first lesion studies inspired by imaging findings, explored whether the right PFC was involved in cued recall by testing left and right frontal damaged patients on a word-stem-cued recall task. They found that, contrary to the imaging evidence, patients with right frontal lesions showed no impairment. They therefore argued that the regions of the right PFC that were activated in PET studies were involved but not necessary for patients to perform the task.

Lee *et al* (2002) also directly compared imaging and lesion methodology by running the same task both with normal subjects in an fMRI scanner, and with unilateral frontal-lobe excision patients. Their task involved the encoding and retrieval of both visual and verbal stimuli. They found that in the scanner, encoding of visual stimuli led to bilateral PFC activation whilst encoding of verbal stimuli led to preferential activation of the left PFC. At retrieval both visual and verbal stimuli led to bilateral PFC activation. In their lesion study they found that patients were significantly impaired compared to controls, but no significant differences between the right and left sided lesioned patients were found. They concluded that the memory related asymmetries observed in functional neuroimaging studies may not be critical for task performance.

So why do patient studies fail to support findings from imaging studies? There are of course many reasons why patient studies may not replicate imaging findings. One possibility is that there may be recovery of function due to neural reorganisation. Alternatively human neuropsychological studies may underestimate the importance of prefrontal regions to episodic memory because they tend to have very small samples sizes. However one of the most important reason why lesion studies have not until now been able to provide support for imaging research is because coarse methods of lesion localisation have been employed.

Previous studies have tended not to distinguish or create subgroups of patients according to precise lesion location. Many have used an undifferentiated "frontal" group, or at best some have divided frontal patients into left frontal and right frontal groups. The mix of

aetiologies is likely to have confused the picture even further. For example it is unclear whether more severe memory deficits such as recognition impairments or false recognition might be specifically associated with medial damage (for example that which follows ACOA aneurysms) rather than with lateral PFC damage. If this is so it may account for the discrepant findings between some studies. If specific prefrontal regions make different contributions to episodic memory performance (as has been implied by imaging findings), such effects may have been obscured by the variability of lesion locations in group analyses.

Stuss and his colleagues (Stuss, Alexander, Floden, Binns, Levine, McIntosh, Rajah & Hevenor, 2002) have developed a new method of analysing lesion location in brain damaged patients which allows clearer links to be made between specific areas of damage in the human frontal lobes and the different impairments that are sometimes seen following frontal damage. This method allows a far more precise attempt at functional localisation in the brain, compared to previous methods which have only allowed gross divisions to be made. They use anatomical classifications based on Petrides & Pandya's (1994) architectonic divisions. These detailed architectonic areas are then grouped into regional subgroupings, and then into four major anatomical regions: polar, inferior medial, superior medial and lateral. Later, for the purposes of analysis, each patient's lesion can be described at one of three levels of specificity: 1) the cytoarchitectonic level (52 areas), 2) the regional level (20 areas) or 3) the surface level (8 areas) according to the level of detail required. Statistical analysis can then proceed by a number of methods, either by traditional anatomical grouping methods, or by a variety of other statistical procedures which essentially correlate the types of behavioural impairment shown by each patient with the areas of damage as seen on their scan. Stuss's group have also pioneered approaches which reverse the traditional methods of analysis by grouping first in terms of behavioural performance and then looking at the corresponding areas of damage in these impaired patients. The success of this approach in discovering more precise frontal lobe-functional relationships has been demonstrated in a series of studies investigating traditional frontal lobe tasks as well as attention, learning and memory (Alexander *et al*, 2003; Stuss *et al*, 1994; Stuss, Alexander, Hamer, Palumbo, Dempster,

Binns, Levine & Izukawa, 1998; Stuss, Alexander, Shallice, Picton, Binns, MacDonald, Borowiec & Katz, in press; Stuss, Binns, Murphy & Alexander, 2002; Stuss, Bischop, Alexander, Levine, Katz & Izukawa, 2001a; Stuss, Floden, Alexander, Levine & Katz, 2001b; Stuss, Levine, Alexander, Hong, Palumbo, Hamer, Murphy & Izukawa, 2000; Stuss, Murphy, Binns & Alexander, 2003).

This thesis aims to investigate the functional and anatomical contributions of the prefrontal cortex to memory performance in a sample of 42 patients with focal frontal lobe lesions. In order to investigate specific lesion-behaviour relationships, lesion localisation and statistical procedures developed from those of Stuss *et al* (2002) will be employed to analyse performance on a range of standardised and newly developed experimental tests addressing memory processes highlighted in previous imaging and neuropsychological research. This also allows direct comparisons to be made with findings from neuroimaging.

Several questions are addressed. Both lateral frontal lobe damage and more medial damage resulting from ACOA aneurysms have been associated with memory problems and confabulation, and both have been attributed to frontal executive difficulties. This thesis explores which specific memory processes are impaired in frontal patients. Are the deficits secondary to impairments at encoding or at retrieval? Are they specific to particular types of memory task (e.g. recall vs recognition)? And does the pattern of memory impairment depend on the precise area of damage? If it does, does the prefrontal cortex lateralise according to encoding vs retrieval, according to stimulus modality, or according to the type or complexity of the processing being carried out? Furthermore which additional factor is it (anatomically and functionally) that leads to confabulation, the most extreme form of frontal memory impairment?

In order to address these questions the thesis proceeds in the following form. Chapter 2 describes the characteristics of the sample, the lesion localisation procedures, and outlines the approach to statistical analysis adopted. Chapter 3 presents the results of a series of baseline neuropsychological tests of general executive functioning and memory.

In Chapter 4 we address whether confabulation is present in the sample. If it is, which specific regions of the frontal lobes are critical for confabulation to occur, and in response to which types of questioning does it arise? Chapter 5 investigates the performance of the sample on two experimental tests of recall. It examines whether impairments are different for visual and verbal information, whether they are a result of deficits at the encoding or retrieval stage, and whether they occur in conjunction with intrusion errors and monitoring impairments. Chapter 6 specifically investigates the involvement of the left frontal lobe at encoding. Imaging studies have indicated that the left frontal lobe (and specifically the left IFG) is involved in the retrieval or use of semantic information at encoding. However one recent theory proposes that it is specifically involved in the selection of semantic attributes from competing alternatives rather than retrieval of semantic information *per se* (Thompson-Schill *et al*, 1997, 1999). The experiment reported here tests this prediction from imaging in a neuropsychological sample. Chapter 7 investigates reality monitoring processes in the sample, on the basis of evidence that the frontal lobes may be critical for this process, and that failure may be specifically associated with confabulation (Johnson 1997; Johnson *et al*, 1997). Chapters 8 and 9 focus on the theory of spontaneous confabulation proposed by Schnider and colleagues (Ptak *et al*, 2001; Ptak & Schnider, 1999; Schnider, 2001; Schnider *et al*, 1996a,b, 2000a,b, 2002; Schnider & Ptak, 1999; Treyer *et al*, 2003). Specifically, Chapter 8 investigates the suppression of previous associations in the sample in a continuous recognition task based on that developed by Schnider & Ptak (1999), and investigates whether performance on the task does indeed distinguish between confabulating and non-confabulating frontal patients. In Chapter 9 a detailed case study of three confabulating patients is presented exploring the mechanisms underlying failure on this task, and proposing possible additional mechanisms underlying confabulation.

CHAPTER TWO:
PARTICIPANTS, LESION ANALYSIS & STATISTICAL METHODS

2.1 PARTICIPANTS:

74 patients with focal lesions were recruited from the National Hospital for Neurology and Neurosurgery. The inclusion and exclusion criteria were 1) the presence of a focal lesion confined to frontal or non-frontal brain regions, 2) English as a first language, 3) absence of childhood-onset epilepsy (late onset seizures arising from the lesion were allowed), 4) absence of severe aphasia, and 5) absence of other significant neurological and psychiatric disorders.

58 of these patients had focal frontal lesions. However 16 of these were excluded at the scan analysis stage either because they did not have MRI or CT available for analysis, the scan was not clear enough to complete a detailed protocol or because significant posterior involvement was found. This left a group of 42 frontal patients; 23 male and 19 female, with a mean age of 48.62 ± 15.96 years and mean years of education 13.06 ± 3.05.

16 patients with posterior lesions were assessed, one of whom was excluded as additional frontal damage was found when her scans were examined. This left a group of 15 posterior patients; 7 male and 8 female, with a mean age of 52.33 ± 17.27 years and mean years of education 11.87 ± 2.95. Of these 9 had lesions of the temporal lobe, 3 had lesions of the parietal lobe, 2 had parieto-occipital lesions, and 1 had a tempero-parietal lesion. A description of patients' lesion location, aetiology and chronicity is presented in table 2.2.

50 healthy adult controls with no history of neurological or psychiatric illness were recruited from a subject pool and from posters in the hospital and surrounding area. This group consisted of 25 male and 25 female participants, with a mean age of 48.36 ± 14.24 years and mean years of education 12.93 ± 3.33. One way analysis of variance confirmed that the Frontal, Posterior and Control groups did not differ significantly in terms of age

($F_{(2, 104)} = 0.40$, $p = 0.67$) or years of education ($F_{(2, 104)} = 0.85$, $p = 0.43$). The Frontal and Posterior groups did not differ in terms of chronicity ($t_{(50)} = 0.75$, $p = 0.46$).

All participants, patients and healthy controls, were assessed using a battery of tests comprising baseline neuropsychological assessment and the 6 experimental tests. The battery was given in a fixed order to all participants and took between three and four hours to administer. Participants were tested either at hospital or in their homes following discharge, and testing was conducted in between one and four sessions (with breaks when required) depending on fatigue. All participants gave informed consent to take part in the study, and were allowed to withdraw at any time. In some cases it was not possible to complete the full battery, for example when a patient was discharged home far from the hospital where it was not possible to follow them up, or where a patient decided not to continue with the study. The number of patients assessed on each test is always stated in the relevant results table.

2.2 LESION ANALYSIS:

Analysis of lesion site amongst the frontal patients was conducted following Stuss *et al* (2002). MRI scans (or CT scans if MRI was unavailable) were examined and patients were coded for the presence or absence of lesion in 12 regional areas in each hemisphere (24 coded areas in total). An area was only coded as damaged if at least 25% of that area was affected. These could be broadly grouped into three surface areas: Inferior Medial, Superior Medial and Lateral. Table 2.1 shows how these groupings were comprised, along with approximate equivalent Brodmann areas.

Table 2.1:
Levels of Lesion Specification (after Stuss et al, 2002)

SURFACE (Grouping Level 3)	(Grouping Level 2)	REGION	CYTOARCHITECTURE
INFERIOR MEDIAL	ORBITAL	1) Orbital	11, 25
	MEDIAL	2) Sub Genu	25
		3) Anterior Section of Cingulate	32, 24
		4) Posterior Section of Cingulate	24, 23
SUPERIOR MEDIAL	MEDIAL	1) Anterior Section of Superior Frontal Gyrus (Medial Surface)	10, 8, 6
		2) Posterior Section of Superior Frontal Gyrus (Medial Surface)	6
LATERAL	LATERAL	1)Anterior Section of Superior Frontal Gyrus (Lateral Surface)	10, 9, 8
		2)Posterior Section of Superior Frontal Gyrus (Lateral Surface)	8, 6
		3)Anterior Section of Middle Frontal Gyrus	8, 9, 46
		4)Posterior Section of Middle Frontal Gyrus	8, 6
		5)Anterior Section of Inferior Frontal Gyrus	47, 45
		6)Posterior Section of Inferior Frontal Gyrus	45, 44

A radiologist blind to the nature of the deficit observed in the patients classified frontal lesion sites according to sulci and gyri rather than according to the Petrides and Pandya (1994) architectonic divisions used by Stuss *et al* (2002) to ensure accuracy. Although sulci and gyri are not functional divisions they are the most reliable method of anatomical localisation across a number of patients. This allowed groupings into the three surface areas shown (Inferior Medial, Superior Medial and Lateral) but did not allow accurate divisions of the polar area to be made as was the case in Stuss *et al* (2002). Areas of oedema were coded in initial analysis, but were not common enough across patients to be included in later analysis. Divisions were made as follows: On the medial surface, the superior / inferior border was taken at the division between the superior frontal gyrus and the cingulate gyrus. The anterior / posterior border on the medial surface was taken as the midway point between the frontal pole and the ramus marginalis. The anterior / posterior border on the lateral surface was taken at the midway point between the frontal pole and the precentral sulcus.

Table 2.2:
Lesion Location, Aetiology and Chronicity within Patient Groups

Participant No.	Lesion location	Aetiology	Chronicity (days)
Orbital			
102	IMonly.	ACoA	1830
108	IMonly.	ACoA	8
110	IMonly.	AVM	4
112	IMonly.	Haemotoma	18
118	IMonly.	Meningioma	355
123	IMonly.	ACoA	150
130	Insufficient detail from MRI.	ACoA	8
141	IMonly.	ACoA	7
142	IMonly.	Intracerebral haemorrhage	8
143	IMonly.	ACoA	16
148	SMIM, LLat, RLat.	Abscess	10
155	Insufficient detail from MRI.	ACoA	3
Medial			
103	SMIM.	Low grade glial tumour	5
105	IMonly.	ACoA	3
115	SMIM, RLat.	Haemotoma	5
117	SMIM, RLat.	Oligoastrocytoma	5
126	SMIM, RLat.	Metastasis	3
144	SMIM.	Astrocytoma	210
145	IMonly.	ACoA	17
150	SMIM.	ACoA	7
Left Lateral			
106	IMonly, LLat.	Meningioma	5
109	SMIM, LLat.	Astrocytoma	3
120	IMonly, LLat.	Haemotoma	7
122	IMonly, LLat.	ACoA	21
134	SMIM, LLat.	Glioblastoma	4
137	LLat.	Metastasis	4
138	IMonly, LLat.	Glioma	3
139	LLat.	Glioma	4
154	IMonly, LLat.	Glioma	80
Right Lateral			
111	RLat.	Meningioma	4
114	SMIM, RLat.	Meningioma	7
119	RLat.	Chronic Subdural Haemotoma	14
121	RLat.	Meningioma	3
125	RLat.	Glioblastoma	36
127	SMIM, RLat.	Meningioma	25
135	RLat.	Astrocytoma	6
147	RLat.	Meningioma	23
156	RLat.	Meningioma	461
Unclassified frontal patients (included in third analysis)			
131	SMIM, LLat.	ACoA	8755
133	SMIM, LLat.	Glioma	22
136	IMonly, LLat.	Lymphoma	5
146	IMonly, LLat.	Astrocytoma	54
Posterior			
201	Right Temporal	Glioblastoma	4

202	Left Temporal	Astrocytoma	5
203	Left Temporal	Cystic Glioma	4
204	Left Temporal	Oligodendroglioma	2
205	Right Temporal	Glioma	4
206	Right Parietal	Meningioma	25
207	Left Temporal	Glioma	2
208	Left Temporal	Lobectomy	2
209	Right Tempero-parietal	Glioblastoma	6
210	Left Parietal	Glioma	5
211	Left Parieto-Occipital	Meningioma	463
212	Left Temporal	Apendymoma	36
213	Left Tempero-Parietal	Mixed oligodendroglioma and astrocytoma	20
214	Left Parietal	Meningioma	23
216	Left Tempero-Parietal	Meningioma	3

2.3 APPROACH TO ANALYSIS:

Analysis of the series data for all behavioural measures was undertaken with three parallel approaches.

Grouping / Analysis Level 1:

Univariate ANOVAs were used to compare the Controls against the Frontal and Posterior patient groups.

Grouping / Analysis Level 2:

Secondly the frontal group were divided into four subgroups according to the primary site of their lesion: Right Lateral, Left Lateral, Orbital or Medial. Patients could only be included in one group (see table 2.2). 38 patients were included in this analysis. Four were excluded as they had lesions that were too extensive to be accurately assigned only to one grouping – there was no obvious largest area of damage in these patients. This gave groups of 12 Orbital, 9 Left Lateral, 9 Right Lateral and 8 Medial patients. Univariate ANOVAS were employed to compare these four groups against the control group. The Posterior group was excluded in this analysis.

Covariates:

In the first two levels of analysis age and years of education were included as covariates, and these results are reported where significant. Current intellectual functioning was estimated using Ravens Advanced Progressive Matrices (APM) and premorbid functioning using the National Adult Reading Test (NART). Analysis revealed that the

frontal group did differ from the control group on the APM (see Chapter 3). However since there are good reasons to assume that any effect on this test may be an effect of the frontal lesion itself it would be inappropriate to routinely covary for APM performance. No significant differences were found between male and female performance on any variable within the control group, so this was ignored in subsequent analyses (with two exceptions in baseline tests, discussed in Chapter 3).

Grouping / Analysis Level 3:

Our third approach employed a different grouping system. Frontal patients were coded according to whether they had damage in four regions (derived from Table 2.1). The four regions were:

1) Inferior Medial Only (IMonly).

   Patients with inferior medial damage only, excluding superior medial damage. This region was defined as including the orbital region, the sub genu, and the anterior and posterior sections of the anterior cingulate (see Table 2.1)

2) Superior Medial (SMIM)

   Patients with superior medial damage (those who had inferior medial damage in addition to their superior medial damage were also included here). The superior medial region was defined as including the anterior and posterior sections of the superior frontal gyrus on the medial surface (see Table 2.1)

3) Left Lateral (LLat)

   Patients with damage affecting the anterior and posterior sections of the superior frontal gyrus on the lateral surface, the anterior and posterior sections of the middle frontal gyrus, and the anterior and posterior sections of the inferior frontal gyrus on the left side were included in this group (see Table 2.1).

4) Right Lateral (RLat)

   Patients with damage affecting the anterior and posterior sections of the superior frontal gyrus on the lateral surface, the anterior and posterior sections of the middle frontal gyrus, and the anterior and posterior sections of the inferior frontal gyrus on the right side were included in this group (see Table 2.1).

40 frontal patients were included in this third stage of analysis. Two were excluded as there was insufficient clarity in their MRI scans to provide a sufficiently detailed analysis of the extent and region of their lesions. In this analysis patients could be included in more than one group if their lesions encompassed more than one area. This yielded groups of the following sizes: IMonly n = 18, SMIM n = 13, LLat n = 14 and RLat n = 13. Within each group those patients who had damage in that area were compared to those patients without damage in that area with independent samples t-tests.

See tables 2.3 and 2.4 for a breakdown of the degree of overlap between these two grouping methods.

Table 2.3:
Probability of classification in level 3 groupings as a function of level 2 groupings.
NB. Rows in this table may not total 1 as membership of more than one group is possible

		Grouping / Analysis Level Three			
		IMOnly	SMIM	LLat	RLat
Grouping/ Analysis Level Two	Orbital	0.75	0.08	0.08	0.08
	Medial	0.25	0.75	0.0	0.375
	Left Lateral	0.55	0.22	1.0	0.0
	Right Lateral	0.0	0.22	0.0	1.0
	Unspecified	0.5	0.5	1.0	0.0

Table 2.4:
Probability of classification in level 2 groupings as a function of level 3 groupings.

		Grouping / Analysis Level Two				
		Orbital	Medial	Left Lateral	Right Lateral	Unspecified
Grouping/ Analysis Level Three	IMOnly	0.5	0.11	0.28	0.0	0.11
	SMIM	0.08	0.46	0.15	0.15	0.15
	RLat	0.08	0.23	0.0	0.69	0.0
	LLat	0.07	0.0	0.64	0.0	0.29

Transformations and Statistical Tests Employed:

In all cases where Levene tests showed that the error variances between the groups differed significantly, data were transformed using the arcsin transformation for proportion data, and the natural log transformation in all other cases. If error variances remained unequal after this transformation then one of two approaches was used. With analysis by ANOVA (Grouping / Analysis Levels 1 and 2), non-parametric statistics were

applied to the data (Kruskal-Wallis test). For analysis by t-test (Grouping / Analysis Level 3), analyses using adjusted degrees of freedom to correct for unequal variance are reported.

Post Hoc Testing And Correction For Multiple Comparisons:

Significant ANOVAS were followed by pairwise comparisons to look for differences between the groups. In the absence of an accepted method for making post hoc comparisons following a significant Kruskal-Wallis test, pairwise Mann Whitney U tests were conducted as recommended by Dytham (2003). This method has exactly the same logic as the LSD tests if it is only applied when the Kruskal-Wallis test gives a significant result.

Adjustment for multiple comparisons was made according to the following rule. In analysis level 1 (Control vs Frontal vs Posterior) non-corrected significance levels are reported but are only treated as significant if they achieve $p<=0.017$ (Bonferroni correction for three comparisons). If this shows a significant Frontal effect, then Bonferroni corrections are not applied to the second level of analysis which further explores the Frontal effect (Orbital vs Medial vs Left Lateral vs Right Lateral vs Control). This is because the aim of this level of analysis is to be more specific anatomically about a lesion effect already established in the previous analysis. If this second level of analysis gives significant results where the first level did not reveal a deficit in the frontal group, they are reported only if they achieve $p<= 0.013$ (Bonferroni correction for four comparisons, each Frontal group against Controls).

T-test results from the third level of analysis are only reported if the initial analysis shows a Frontal effect. If findings from these multiple levels of analysis are consistent then it may be argued that strong conclusions can be drawn from the data despite multiple comparisons.

CHAPTER THREE:
BASELINE NEUROPSYCHOLOGICAL ASSESSMENT

All participants were given a range of standard neuropsychological tests to assess their baseline functioning, including measures of intellectual functioning, language and visual perception. They were also given standardized tests of executive functioning and memory. The results of these baseline assessments are presented below.

3.1 GENERAL BASELINE TESTS

3.1.1 General Intellectual Functioning:

Raven's Advanced Progressive Matrices (APM; Raven, Raven & Court, 1998) was administered as a measure of general intelligence. Mean age-scaled scores for the Control, Frontal and Posterior groups are presented in Table 3.1.

Table 3.1:
Mean Age-Scaled Scores for Raven's Advanced Progressive Matrices

	Frontal	Posterior	Control
N	42	14	50
Mean Score (SD)	9.36 (3.38)	8.14 (4.57)	11.18 (2.85)

Analysis of variance revealed a significant effect of group ($F_{(2, 101)} = 5.57$, $p = 0.005$), with a significant covariate of years of education ($F_{(1, 101)} = 9.39$, $p = 0.003$). Pairwise comparisons confirmed that the Control group had significantly higher APM scores than both the Frontal ($p = 0.009$) and the Posterior group ($p = 0.007$). This result is not surprising in the light of recent suggestions that general fluid intelligence as measured by the APM may have its neurobiological basis in the left lateral PFC and bilateral parietal regions (Gray, Chabris & Braver, 2003). However no further differences were found within the Frontal group in subsequent analyses (see Appendix 1, refs 2.1, 3.1, 4.1, 5.1, 6.1).

3.1.2 Language Skills:

The National Adult Reading Test (NART; Nelson, 1982) was also administered as a measure of language functioning and pre-morbid intelligence.

Table 3.2:
Mean NART-Derived Full-Scale IQ.

	Frontal	Posterior	Control
N	39	13	50
Mean FSIQ (SD)	104.46 (15.16)	100.08 (11.88)	110.64 (9.78)

Analysis of variance revealed a significant effect of group ($F_{(2, 97)} = 4.76$, $p = 0.011$), with significant covariates of age ($F_{(1, 97)} = 4.23$, $p = 0.042$) and years of education ($F_{(1, 97)} = 28.34$, $p = 0.000$). Levene's test for equality of error variances was significant ($F_{(2, 99)} = 3.15$, $p = 0.047$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference ($\chi^2 = 8.29$, $df = 2$, $p = 0.016$). Pairwise Mann-Whitney U comparisons confirmed that the Posterior group had a significantly lower premorbid IQ than the Control group ($U = 172.50$, $p = 0.01$). The depressed NART performance in our Posterior group may be explained by the possible presence of mild dyslexia and aphasia in this group. Analysis at level 2 also failed to reveal any frontal effects on the NART (see Appendix 1, ref 2.2), confirming that there was no significant language or premorbid IQ impairment in the frontal group.

The Graded Naming Test (GNT; McKenna & Warrington, 1983) was administered as a measure of confrontation naming ability.

Table 3.3:
Mean Age-Scaled GNT Scores.

	Frontal	Posterior	Control
N	39	12	50
Mean (SD)	9.56 (3.75)	10.08 (2.70)	11.04 (3.49)

Analysis of variance revealed no significant difference of group on naming ability ($F_{(2, 96)} = 1.94$, $p = 0.149$), confirming that there were no basic naming problems amongst our series, a result that was expected given our exclusion criteria. Analysis at level 2 also failed to reveal any significant Frontal Subgroup effects (see Appendix 1, ref 2.3).

3.1.3 Visual Perception:

To ensure that there were no basic perceptual difficulties amongst our patients, the Incomplete Letters Subtest from the Visual Object and Space Perception Battery (VOSP; Warrington & James, 1991) was administered.

Table 3.4:
Mean Incomplete Letters Score (Max =20).

	Frontal	Posterior	Control
N	40	14	50
Mean (SD)	19.08 (1.49)	19.29 (0.91)	19.26 (0.88)

Analysis of variance revealed no significant effect of group ($F_{(2, 99)} = 0.12$, $p = 0.89$), confirming that there were no basic visual perceptual deficits in our series. Analysis at level 2 also failed to reveal any significant Frontal Subgroup effects (see Appendix 1, ref 2.4).

3.1.4 Interim Summary: General Baseline Functioning in the Sample:

General baseline neurological assessment supported the position that there were no language or visual perception impairments in the frontal group, so these factors will be excluded as possible confounds. There was a slight reduction in Ravens APM performance which may itself be an effect of frontal damage and is consistent with evidence suggesting that general fluid intelligence may have its neurobiological basis in the left lateral PFC and bilateral parietal regions (Gray *et al*, 2003).

3.2 STANDARDISED MEASURES OF EXECUTIVE FUNCTION

Five standardised measures of executive function were employed to give an estimate of frontal/executive function in the sample.

3.2.1 Stroop Task:

The Stroop task (Stroop, 1935; Trenarry, Crosson, DeBoe & Leber, 1989) is frequently used to assess frontal / executive function as it provides a measure of the ability to shift between competing response modes and conflicting perceptual sets. It demands the ability to suppress a habitual response in favour of a more unusual one. The Trenarry *et al* (1989) version of the Stroop task consists of two sets of 112 colour names printed in non-matching coloured inks. With the first set participants are asked to read out the colour words (word condition), and with the second they are asked to name the colour of the ink (colour-word condition). Both conditions should be completed as fast as possible with the minimum number of errors possible. Three measures are reported for each condition: 1) the time taken to complete all 112 items (Word or Colour-Word Time), 2) the number of errors committed (Word or Colour-Word Errors), and 3) the number of items completed correctly in 120 seconds (Word or Colour-Word Score).

Table 3.5:
Mean Response Times, Error Rates and Standardised Scores for Word and Colour-Word Conditions of the Stroop Task

	Frontal	Posterior	Control
Word Time (s) Valid N	71.06 (29.88) 35	68.00 (22.05) 12	53.71 (10.73) 48
Word Errors Valid N	0.11 (0.52) 36	0.17 (0.39) 12	0.06 (0.24) 49
Word Score/112 Valid N	110.75 (6.06) 36	111.83 (0.39) 12	111.96 (0.20) 49
Colour-Word Time (s) Valid N	216.43 (153.37) 28	145.25 (57.70) 12	132.81 (33.12) 48
Colour-Word Errors Valid N	8.50 (19.21) 32	3.17 (8.48) 12	1.02 (1.98) 49
Colour-Word Score / 112 Valid N	75.64 (71.06) 36	96.25 (18.66) 12	99.96 (16.32) 49

Univariate analysis of variance revealed a significant effect of group on three of these measures (see Appendix 1 refs 1.1, 1.2, 1.3, 2.5, 2.6, 2.7 for insignificant results).

Word Time:

Firstly there was a significant effect of group on Word Time ($F_{(2, 90)} = 7.58$, $p = 0.001$). Levene's test for equality of error variances was significant ($F_{(2, 97)} = 8.50$, $p = 0.000$).

However a subsequent Kruskal-Wallis test confirmed the significance of the group difference (χ^2 = 14.02, df = 2, p = 0.001). Pairwise Mann Whitney U comparisons confirmed that both the Frontal group (U = 463.50, p = 0.001) and the Posterior group (u = 162.50, p = 0.02) were significantly slower to complete this condition than the Control group.

Further exploration of whether the Frontal deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.6:
Mean Response Times for Word Condition: Grouping / Analysis Level 2.

	Orbital	Medial	Left Lateral	Right Lateral	Control
Word Time (s)	53.78 (15.30)	91.00 (47.48)	60.75 (18.97)	74.25 (24.53)	53.71 (10.73)
Valid N	9	6	8	8	48

Analysis of variance revealed a significant effect of Frontal Subgroup on Word Time ($F_{(4, 72)}$ = 6.93, p = 0.000). Pairwise comparisons confirmed that the Medial (p = 0.000) and Right Lateral (p = 0.005) groups were significantly slower to complete the word condition than the Control (p = 0.000) group.

The third level of analysis did not reveal any further significant results (See Appendix 1 refs 3.2, 4.2, 5.2, 6.2).

Colour-Word Time:

Univariate analysis of variance also revealed a significant effect of Group (Control, Frontal or Posterior) on Colour-Word Time ($F_{(2, 83)}$ = 8.15, p = 0.001), with a significant covariate of age ($F_{(1, 83)}$ = 22.46, p = 0.000). Levene's test for equality of error variances was again significant ($F_{(2, 97)}$ = 8.50, p = 0.000). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference (χ^2 = 7.12, df = 2, p = 0.028). Pairwise Mann Whitney U comparisons confirmed that the Control group was significantly faster than the Frontal group (U = 426.50, p = 0.008).

Further exploration of whether this Frontal deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.7:
Mean Response Times for Colour-Word Condition: Grouping / Analysis Level 2.

	Orbital	Medial	Left Lateral	Right Lateral	Control
Colour-Word Time (s)	157.5	117.25	298.20	248.86	132.81
SD	(63.87)	(15.61)	(245.12)	(176.98)	(33.12)
Valid N	8	4	5	7	48

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(4, 65)} = 5.09$, $p = 0.001$) with a significant covariate of age ($F_{(1, 65)} = 19.30$, $p = 0.000$). Levene's test for equality of error variances was again significant ($F_{(4, 67)} = 6.71$, $p = 0.000$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference ($\chi^2 = 9.75$, $df = 4$, $p = 0.045$). Pairwise Mann Whitney U comparisons confirmed that the Right Lateral group was significantly slower than the Control group ($U = 66$, $p = 0.008$). (Although the Left Lateral group also appeared to be impaired on this measure, the difference did not reach significance, presumably because of the small sample size and large SD in this group)

Analysis at the third level revealed the following results.

Table 3.8:
Mean Response Times for Colour-Word Condition: Grouping / Analysis Level 3.

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 10 265.70 (176.96)	N = 8 130.50 (37.04)	N = 10 265.90 (194.46)	N = 10 206.60 (160.59)
Area Not Damaged Mean Score (SD)	N = 16 197.69 (142.54)	N = 18 265.33 (172.32)	N = 16 197.56 (128.06)	N = 16 234.63 (158.77)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients without SMIM damage were significantly slower to complete the colour-word condition then those with SMIM damage. ($t_{(23.13)} = 3.22$, $p = 0.004$; results reported are corrected for unequal variances).

Colour-Word Score:

The third Stroop measure to yield a significant group difference was Colour-Word Score ($F_{(2, 92)} = 10.63$, $p = 0.000$) with a significant covariate of age ($F_{(1, 92)} = 28.80$, $p = 0.000$). Levene's test for equality of error variances was significant ($F_{(2, 94)} = 4.07$, $p = 0.020$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference ($\chi^2 = 9.23$ df = 2, $p = 0.01$). Pairwise Mann Whitney U comparisons confirmed that the Control group obtained significantly higher scores in this condition than the Frontal group ($U = 548.50$, $p = 0.003$)

Further exploration of whether this Frontal deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.9:
Mean Colour-Word Score: Grouping / Analysis Level 2.

	Orbital	Medial	Left Lateral	Right Lateral	Control
Colour-Word Score / 112	90.00 (23.48)	87.00 (40.79)	68.88 (40.62)	69.29 (34.99)	99.96 (16.32)
Valid N	10	7	8	7	49

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(4, 74)} = 4.25$, $p = 0.004$) with a significant covariate of age ($F_{(1, 74)} = 20.99$, $p = 0.000$). Pairwise comparisons confirmed that the Control group obtained significantly higher scores than the Left Lateral ($p = 0.002$), and Right Lateral ($p = 0.011$) groups.

Analysis at the third level revealed the following results.

Table 3.10:
Mean Colour-Word Scores: Grouping / Analysis Level 3.

	IMOnly	SMIM	LLat	RLat
Area Damaged	N = 15	N = 11	N = 13	N = 11
Mean Score (SD)	64.73 (36.06)	88.36 (33.03)	64.08 (38.63)	82.82 (33.18)
Area Not Damaged	N = 19	N = 23	N = 21	N = 23
Mean Score (SD)	80.42 (34.41)	66.39 (35.08)	79.33 (33.02)	69.04 (36.41)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with SMIM

damage obtained significantly higher scores than those without SMIM damage ($t_{(32)} = -2.08$, $p = 0.046$).

In summary, our results indicated that the Medial group showed a significant slowing effect on the word condition of the Stroop task. The Right Lateral group showed significant slowing on both the word and colour-word conditions. For the interference measure (colour-word score) Left Lateral and Right Lateral patients showed impairment. Medial patients were not impaired, and this was further corroborated by the finding that SMIM damaged patients were preserved on both colour-word time and colour-word score.

Our findings are consistent with previous studies that have identified either left (Perret, 1974; Regard, 1981, Taylor, Kornblum, Lauber, Minoshima, & Koeppe, 1997), right (Vendrell, Junque, Pujol, Jurado, Molet & Grafman, 1995) or bilateral (Leung, Skudlarski, Gatenby, Peterson & Gore, 2000; Peterson, Kane, Alexander, Lacadie, Skudlarski, Leung, May & Gore, 2002; Zysset, Muller, Lohmann & Yves von Cramon, 2001) frontal areas as critical for Stroop performance. However it is in marked contrast to a series of imaging (Bench, Frith, Grasby, Friston, Paulesu, Frackowiak & Dolan, 1993; Leung *et al*, 2000; Pardo, Pardo Janer & Raichle, 1990; Peterson *et al*, 2002) and neuropsychological studies (Holst & Vilkki, 1988; Swick & Jovanovic, 2002; Vendrell *et al*, 1995) that have identified the superior medial PFC, and specifically the anterior cingulate cortex, as critical for Stroop task performance. Stuss *et al* (2001a) reported a general slowing effect in their left and right lateral patients across conditions, consistent with our results, but concluded that bilateral superior medial regions (interestingly *excepting* the anterior cingulate) were the critical regions for errors in the colour-word condition of the Stroop task. Our results, consistent across all levels of analysis, contrast sharply with this, strongly indicating that the medial region is *not* involved in the Stroop interference task. However as the numbers in each group are small it would be premature to treat this evidence as a refutation of the medial involvement in the Stroop task.

Our finding that the orbital frontal region is not implicated in Stroop performance differs from imaging studies which have activated this area (Bench *et al*, 1993; Leung *et al*, 2000; Peterson *et al*, 2002; Zysset *et al*, 2001) but is consistent with neuropsychological evidence which has consistently reported that damage in this area has no detrimental effect on Stroop performance (Stuss, 1991; Stuss *et al*, 2001a).

3.2.2 Trail-Making Test:

The Trail-Making Test (TMT; Reitan & Wolfson, 1988) is frequently used to assess frontal / executive dysfunction as impairment (particularly on part B) is assumed to reflect difficulties in executing and modifying a plan of action, or in maintaining two trains of thought at once. Part A requires the subject to draw a line joining a series of 25 encircled numbers randomly arranged on a page in the correct order. Part B requires joining of 25 encircled numbers and letters in alternating order. The test therefore relies on rapid visual search, visuospatial sequencing and cognitive set shifting.

The most frequently used measure of performance on the TMT is time to complete each part. However Stuss *et al* (2001b) have suggested that error analysis is a more useful method of categorizing performance. Therefore both mean completion times and error rates are employed in the following analyses.

Table 3.11 shows mean completion times and error rates for parts A and B.

Table 3.11:
Mean Completion Times and Error Rates on Parts A and B of the Trail Making Test

	Frontal	Posterior	Control
Mean Part A Time (SD) Valid N	52.87 (33.88) 38	42.58 (19.90) 12	30.38 (10.27) 50
Mean Part A Errors (SD) Valid N	0.29 (0.57) 38	0.00 (0.00) 12	0.16 (0.42) 50
Mean Part B Time (SD) Valid N	129.67 (101.73) 36	95.83 (48.62) 12	69.90 (29.07) 50
Mean Part B Errors (SD) Valid N	0.86 (1.94) 36	0.58 (1.44) 12	0.44 (0.61) 50

Univariate analysis of variance revealed a significant effect of group on both of the time measures (see Appendix 1 refs 1.4, 1.5, 2.8, 2.9 for insignificant error measure results).

Part A Time:

There was a significant effect of group on time to complete part A ($F_{(2, 95)} = 15.54$, $p = 0.000$) with a significant covariate of age ($F_{(1, 95)} = 18.66$, $p = 0.000$). Pairwise comparisons confirmed that the Control group was significantly faster to complete this condition than the Frontal group ($p = 0.000$).

Further exploration of whether this Frontal deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.12:
Mean Completion Times for Trail Making Test Part A: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
Mean Completion Time (SD)	N = 11 37.18 (12.71)	N = 8 64.13 (49.87)	N = 7 48.29 (27.02)	N = 8 58.38 (29.52)	N = 50 30.38 (10.27)

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(4, 77)} = 9.86$, $p = 0.000$) with a significant covariate of age ($F_{(1, 77)} = 3.05$, $p = 0.000$). Levene's test for equality of error variances was significant ($F_{(4, 79)} = 3.53$, $p = 0.011$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference ($\chi^2 = 19.83$ df = 4, $p = 0.001$). Pairwise Mann Whitney U comparisons confirmed that the Control group were significantly faster to complete part A than the Medial ($U = 97.5$, $p = 0.021$), Left Lateral ($U = 73.00$, $p = 0.013$), and Right Lateral ($U = 44.00$, $p = 0.000$) groups.

Analysis at the third level revealed no further results (See Appendix 1 refs 3.3, 4.3, 5.3, 6.3).

Part B Time:

There was also a significant effect of group (Control, Frontal or Posterior) on time to complete part B of the trail making test ($F_{(2, 93)} = 13.32$, $p = 0.000$), with significant covariates of age ($F_{(1, 93)} = 22.10$, $p = 0.000$), and education ($F_{(1, 93)} = 4.41$, $p = 0.038$).

Levene's test for equality of error variances was significant ($F_{(2, 95)} = 4.20$, $p = 0.018$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference ($\chi^2 = 14.38$, df = 2, $p = 0.001$). Pairwise Mann Whitney U comparisons confirmed that the Control group was significantly faster to complete this condition than the Frontal group ($U = 471.00$, $p = 0.000$).

Further exploration of whether this Frontal deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.13:
Mean Completion Times for Trail Making Test Part B: Grouping / Analysis Level 2.

	Orbital	Medial	Left Lateral	Right Lateral	Control
	N = 11	N = 7	N = 7	N = 8	N = 50
Mean Completion Time (SD)	78.64 (30.13)	109.00 (53.00)	172.86 (169.01)	153.25 (116.31)	69.90 (29.07)

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(4, 76)} = 7.01$, $p = 0.000$) with a significant covariate of age ($F_{(1, 76)} = 3.46$, $p = 0.000$). Pairwise comparisons confirmed that the Control group were significantly faster to complete part B than the Medial ($p = 0.002$), Left Lateral ($p = 0.000$), and Right Lateral ($p = 0.001$) groups.

Analysis at the third level revealed no further results (See Appendix 1 refs 3.4, 4.4, 5.4, 6.4).

Overall then our analysis showed a consistent slowing of performance of the Medial, Left Lateral and Right Lateral Frontal groups on parts A and B of the test. These results are consistent with those of Stuss *et al* (2001b) when they logarithmically transformed their data (as we have done here). They reported slow performance on part A in their left frontal and right frontal groups, and slowness on part B in all Frontal groups (right, left and bifrontal).

When Stuss *et al* (2001b) analysed the error rates instead of completion times in a more detailed anatomical analysis, they reported that patients with primarily inferior medial

and polar lesions were not impaired on either part of the TMT. Similarly Stuss, Benson, Kaplan, Weir & Della Malva (1981) reported that their orbitofrontal lesion patients were not impaired on the TMT. These studies are consistent with our finding that the Orbital group were the only group who were not significantly impaired on the TMT compared to Controls. Therefore these results taken in conjunction would strongly suggest that the orbital region, in contrast with all other frontal regions, is not critically involved in performance on the TMT. It would seem instead that dorsolateral and superior medial areas may be more critical, a conclusion that is also supported by recent fMRI evidence of activation of the left dorsolateral and medial PFC during performance of a verbal TMT task (Moll, Oliveira-Souza, Moll, Bramati & Andreiuolo, 2002).

3.2.3 FAS Verbal Fluency:

The standard FAS verbal fluency task was also administered as a measure of frontal executive functioning. Participants are asked to produce as many words as they can beginning with a given letter in one minute. Three trials are administered, with the letters F, A and S, and the total number of correct words produced is recorded. Errors are defined as providing proper names, repetitions, intrusions of other letters, and spelling errors.

Table 3.14 shows mean words produced over all three letters, and the mean error rate.

Table 3.14:
Mean number of words produced, and mean number of errors in FAS verbal fluency task.

	Frontal	Posterior	Control
Mean Correct Responses (SD)	27.55 (14.43)	32.31 (11.30)	44.36 (12.25)
Valid N	38	13	50
Mean Errors (SD)	1.72 (1.78)	1.92 (0.95)	1.64 (1.68)
Valid N	36	13	50

Univariate analysis of variance revealed a significant effect of group on the number of correct words produced ($F_{(2, 98)} = 16.74$, $p = 0.000$, see Appendix 1 refs 1.6, 2.10 for insignificant error rate analyses). Levene's test for equality of error variances was

significant ($F_{(2, 100)}$ = 8.66, p = 0.000). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference (χ^2 = 28.34, df = 2, p = 0.000). Pairwise Mann Whitney U comparisons confirmed that the Control group produced significantly more words than the Frontal group (U = 369.50, p = 0.000) and the Posterior Group (U = 161.50, p = 0.005).

Further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.15:
Mean Number Words produced in FAS Verbal Fluency Task: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
Mean Correct Responses (SD)	N = 11 35.91 (13.05)	N = 8 24.25 (11.25)	N = 8 23.38 (14.51)	N = 9 30.33 (14.92)	N = 50 44.36 (12.25)

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(4, 79)}$ = 10.25, p = 0.000). Levene's test for equality of error variances was again significant ($F_{(4, 81)}$ = 2.49, p = 0.05). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference (χ^2 = 25.88 df = 4, p = 0.000). Pairwise Mann Whitney U comparisons confirmed that the Control group produced significantly more words than the Left Lateral (U = 54.50, p = 0.000), Right Lateral (U = 97.50, p = 0.007) and Medial (U = 40.50, p = 0.000) groups.

Analysis at the third level revealed the following results.

Table 3.16:
Mean Number Words produced in FAS Verbal Fluency Task: Grouping / Analysis Level 3

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 22.94 (13.74)	N = 12 26.17 (9.55)	N = 13 21.15 (13.99)	N = 13 31.38 (12.53)
Area Not Damaged Mean Score (SD)	N = 21 29.05 (13.16)	N = 26 26.38 (15.27)	N = 25 29.00 (12.85)	N = 25 23.68 (13.61)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with Left Lateral damage produced significantly fewer words than those patients without Left Lateral damage ($t_{(36)} = 2.05$, $p = 0.047$).

These results suggest that Left Lateral, Right Lateral and Medial damage is associated with reduced output in verbal fluency, with the Left Lateral deficit being most marked and corroborated by the third level of analysis. This is consistent with previous studies that have reported that verbal fluency tasks are most sensitive to lateral frontal lesions (with the emphasis most often on left lateral lesions) in patient investigations (Hecaen & Ruel, 1981; Janowsky *et al*, 1989; Milner, 1964; Perret, 1974; Ramier & Hecaen, 1970) and associated with lateral frontal regions in imaging studies in normal individuals (Cantor-Graae, Warkentin, Franzen & Risberg, 1993; Cuenod, Bookheimer, Hertz-Pannier, Zeffiro, Theodore & LeBihan, 1995; Frith *et al*, 1991; Petersen *et al*, 1988; Warkentin & Passant, 1993; Wise, Chollet, Hadar, Friston, Hoffner & Frackowiak, 1991). Our results are also consistent with a recent sophisticated lesion specificity study by Stuss *et al* (1998) who reported that superior medial damage resulted in moderate impairment on this task, whilst patients with left dorsolateral or striatal damage showed the most dramatic impairment.

Our results also suggest once again than orbital damage does not affect performance on this measure. This is in contrast to Crowe (1992), who identified medial and orbital frontal areas as critical for verbal fluency, but is in line with Stuss *et al* (1998) who reported that damage to the inferior medial frontal region did not affect performance (see also Stuss, Benson, Clermont, Della Malva, Kaplan & Weir, 1986; Warburton, Wise, Price, Weiller, Hadar, Ramsay & Frackowiak, 1996).

3.2.4 Proverbs Task:

A proverb interpretation task was used to assess abstract – concrete thinking, and because it has been reported to be sensitive to frontal lobe damage. Benton (1968) reported very

poor performance in bilateral frontal patients, somewhat better performance among a right frontal group, and relatively good performance among a left frontal group.

Eight common proverbs were read to the participants, and they were asked to explain as best they could what each one meant. A three point scoring system was used, with two points awarded for a full, appropriate and abstract interpretation, 1 point for a partially accurate or concrete interpretation, and 0 for inaccurate interpretations. Mean scores are presented in table 3.17.

Table 3.17:
Mean Proverbs Score for Each Question.

	Frontal	Posterior	Control
Mean Score (SD)	1.09 (0.44)	1.14 (0.44)	1.39 (0.28)
Valid N	38	11	50

Univariate analysis of variance revealed a significant effect of group on proverb interpretation score ($F_{(2, 94)} = 5.50$, $p = 0.006$) with a significant covariate of education ($F_{(1, 94)} = 7.35$, $p = 0.008$). Pairwise comparisons confirmed that the Control group obtained significantly higher scores than the Frontal group ($p = 0.002$). Further analysis did not reveal any significant results (see Appendix 1 ref 2.11). Thus our findings confirmed a general frontal impairment in abstract thinking as measured by interpretation of proverbs, but no further evidence of frontal heterogeneity in this regard.

3.2.5 Sustained Attention:

In light of previous evidence that frontal lobe damage may adversely affect sustained attention (Rueckert & Grafman, 1996; Wilkins, Shallice & McCarthy, 1987), we administered the elevator subtest from the Test of Everyday Attention (TEA; Robertson, Ward, Ridgeway & Nimmo-Smith, 1994). In this task subjects are asked to imagine that they are in an elevator whose floor-indicator is not functioning. They are asked to establish which floor they are on by counting a series of tape-presented tones. The task consists of seven trials, with a score of 7 considered normal, 6 considered doubtful, and five or below definitely abnormal.

Table 3.18:
Mean Scores on the Elevator subtest of the TEA.

	Frontal	Posterior	Control
N	39	11	50
Mean (SD)	6.18 (1.35)	6.45 (1.29)	6.84 (0.42)

Analysis of variance revealed a significant effect of group ($F_{(2, 95)} = 4.80$, $p = 0.01$), with a significant covariate of years of education ($F_{(1, 95)} = 6.27$, $p = 0.014$). Levene's test for equality of error variances was significant ($F_{(2, 97)} = 8.50$, $p = 0.000$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference ($\chi^2 = 9.35$, $df = 2$, $p = 0.009$). Pairwise Mann-Whitney comparisons confirmed that the Control group had significantly higher Elevator scores than the Frontal group ($U = 693.00$, $p = 0.002$).

Further exploration of whether this Frontal deficit might be specific to a particular Frontal Subgroup yielded the following results.

Table 3.19:
Mean Elevator Scores within the Frontal Group: Grouping / Analysis Level 2.

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	8	50
Mean Elevator Score (SD)	6.91 (0.30)	5.25 (1.83)	6.13 (0.99)	6.50 (0.93)	6.84 (0.42)

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(4, 78)} = 8.50$, $p = 0.000$), with a significant covariate of years of education ($F_{(1, 78)} = 5.83$, $p = 0.018$). Levene's test for equality of error variances was again significant ($F_{(4, 80)} = 9.02$, $p = 0.000$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference ($\chi^2 = 22.76$, $df = 4$, $p = 0.000$). Pairwise Mann-Whitney U comparisons confirmed that both the Left Lateral group ($U = 101.50$, $p = 0.002$) and the Medial group ($U = 69.50$, $p = 0.000$) had significantly lower elevator scores than the Controls.

Analysis at the third level revealed no further significant differences (see Appendix 1 refs 3.5, 4.5, 5.5, 6.5).

The Medial and Left Lateral deficits in sustained attention are surprising as deficits in sustained attention have previously been associated with right frontal damage in both imaging (Manly, Owen, McAvinue, Datta, Lewis, Scott, Rorden, Pickard & Robertson, 2003) and neuropsychological (Rueckert & Grafman, 1996; Wilkins *et al*, 1987) studies. To examine the possibility that there may have been right frontal damage in those patients most impaired on this task (despite them falling into different groupings on the basis of major site of lesion), the exact lesion location of 7 frontal patients who scored 5 or below on the task was examined. Three of these patients did have damage restricted to the right hemisphere; all three had right lateral damage, and two had additional right medial damage. However four of the seven patients had damage restricted to the left hemisphere alone with no right hemisphere involvement. All of these four had left medial damage, and three had additional lateral damage. It seems that it is the medial region therefore that is critical in this task, with the left lateral group being impaired due to additional medial involvement. Detailed anatomical analysis of the lesion location amongst the frontal patients in previous studies has not been available, and therefore it is quite possible that the right frontal patients had lesions which extended into the medial area. Indeed the medial deficit in sustained attention reported here is consistent with a recent study (Shallice *et al*, in preparation) that also found a superior medial effect when more sophisticated methods of lesion localisation were employed. It is also consistent with Sarter *et al* (2001, 2003) who have recently proposed a neuronal network mediating sustained attention that includes right medial frontal and right dorsolateral frontal regions, parietal regions, and highlights the crucial role of cholinergic inputs arising from the basal forebrain and noradrenergic projections from the locus coeruleus to the thalamus and basal forebrain (see also Beane & Marrocco, 2004, for similar ideas on the role of the cholinergic system in attention).

3.2.6 Interim Summary: Executive Functioning in the Sample.

Table 3.20
Patterns of impairment on frontal / executive tasks.

TASK	CRITICAL AREAS (SIGNIFICANTLY IMPAIRED COMPARED TO CONTROLS)
STROOP	
Response Time (Word Condition)	Medial, Right Lateral
Response Time (Colour-Word Condition)	Right Lateral (SMIM preserved in level 3 analyses)
Colour-Word Score	Left Lateral, Right Lateral (SMIM preserved in level 3 analyses)
TRAIL-MAKING TEST	
Completion Time Part A	Medial, Right Lateral, Left Lateral
Completion Time Part B	Medial, Right Lateral, Left Lateral
FAS VERBAL FLUENCY	
Number words produced	Left Lateral, Medial, Right Lateral (LLat impaired in level 3 analyses)
TEA SUSTAINED ATTENTION	Medial, Left Lateral

Taken together our assessment of typical frontal / executive tasks amongst our frontal patients has revealed some interesting consistencies (see table 3.20). Most strikingly, we have found no Orbital impairment on any standard measure of executive functioning, in line with other recent studies (Stuss *et al*, 1998, 2001a, b). In contrast we have found Left Lateral, Right Lateral and Medial deficits on most other tasks with the notable exception interference measures on the Stroop task, where striking sparing of the Medial patients was found.

3.3 STANDARDISED MEASURES OF MEMORY

In the light of previous reports of memory impairment, and specifically of disproportionate recall impairment, in frontal lobe patients, several standardised tests of memory were administered.

3.3.1 Recognition:

Two tests were administered to assess recognition abilities in the sample. The Recognition Memory Test (RMT) measured true recognition performance with visual and verbal stimuli. A test of recognition of famous and unknown faces was also administered to assess false facial recognition on the basis of previous evidence associating this phenomenon with right frontal damage.

3.3.1.1 Recognition Memory Test (RMT):

The Recognition Memory Test (RMT; Warrington, 1984) was administered to assess recognition abilities in our sample. The test consists of two-alternative forced choice recognition of two sets of previously encountered stimuli – 50 words, and 50 unfamiliar male faces.

Table 3.21:
Mean RMT Scores for Words and Faces

	Frontal	Posterior	Control
N	41	12	50
Mean Word Score (Max 50)	43.22 (7.21)	41.75 (8.72)	48.22 (1.61)
Mean Faces Score (Max 50)	40.39 (9.57)	36.33 (13.53)	43.86 (5.70)

A mixed model ANOVA with Stimulus Type (words or faces) as the within-subjects variable, and Group as the between subjects variable revealed a significant effect of Group ($F_{(2, 98)} = 11.39$, $p = 0.000$), with a significant covariate of age ($F_{(1, 98)} = 9.64$, $p = 0.002$). There was no effect of Stimulus Type ($F_{(1, 98)} = 2.42$, $p = 0.12$), nor a Group x Stimulus Type interaction ($F_{(2, 98)} = 1.28$, $p = 0.28$). Levene's test for equality of error variances was significant for word score ($F_{(2, 100)} = 10.82$, $p = 0.000$). However a subsequent Kruskal-Wallis test on recall scores for words and faces combined confirmed the significance of the group difference ($\chi^2 = 16.24$, $df = 2$, $p = 0.000$). Pairwise Mann-Whitney U comparisons confirmed that the Control group had significantly higher recognition scores than the Frontal ($U = 640.00$, $p = 0.002$) or the Posterior group ($U = 113.50$, $p = 0.001$).

Further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.22:
Mean RMT Score for Words: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	12	8	8	9	50
Mean Word Score (SD)	46.17 (7.00)	42.50 (6.93)	43.75 (6.04)	42.56 (7.11)	48.22 (1.61)
Mean Faces Score (SD)	44.08 (5.55)	36.50 (16.55)	41.00 (7.60)	41.44 (5.15)	43.96 (5.70)

A mixed model ANOVA with Stimulus Type (words or faces) as the within-subjects variable, and Frontal Subgroup as the between subjects variable revealed a significant effect of Frontal Subgroup ($F_{(4, 80)} = 4.50$, $p = 0.002$), with a significant covariate of age ($F_{(1, 80)} = 7.90$, $p = 0.006$). There was no effect of Stimulus Type ($F_{(1, 80)} = 2.91$, $p = 0.09$), nor a Frontal Subgroup x Stimulus Type interaction ($F_{(4, 80)} = 0.97$, $p = 0.43$). Despite the significant Frontal Subgroup effect pairwise comparisons revealed that no individual frontal subgroup differed significantly from the controls.

Analysis at the third level revealed no further differences (see Appendix 1 refs 3.6, 3.7, 4.6, 4.7, 5.6, 5.7, 6.6, 6.7)

In summary then we found a significant frontal and posterior impairment in recognition for words and faces. It has previously been suggested that frontal patients may have a disproportionate deficit in recall memory tasks whilst their recognition abilities remain intact (Janowsky *et al*, 1989; Jetter *et al*, 1986; Hanley *et al*, 1994; Milner *et al*, 1991; Shimamura *et al*, 1991; Stuss & Benson, 1984). However we can report a significant impairment in recognition abilities in our Frontal group (see also Daum & Mayes, 2000; Delbecq-Derouesne *et al*, 1990; Dimitrov *et al*, 1999; Mayes & Daum, 1997; Schnyer *et al*, 2004; Stuss *et al*, 1994; Wheeler *et al*, 1995). We found no subgroup effects or interactions that would have indicated a specific impairment for verbal material in the Left Lateral group, or for visual material in the Right Lateral group. This is in contrast with previous reports that left frontal patients show a disproportionate impairment in

word recognition compared to right frontal patients on the RMT (Warrington, 1984). However the present results are consistent with evidence that frontal patients as a whole show impairment on both words and faces (Aggleton & Shaw, 1996).

3.3.1.2 False Facial Recognition:

Pathological false recognition has frequently been associated with frontal lobe damage (Budson *et al*, 2002; Curran *et al*, 1997; Delbecq-Derouesne *et al*, 1990; Melo *et al*, 1999; Parkin *et al*, 1996, 1999; Schacter *et al*, 1996; Swick & Knight, 1999; Verfaillie *et al*, 2004; Ward & Parkin 2000). In particular false facial recognition has been reported following right frontal lobe damage by Rapcsak and colleagues (Rapcsak *et al*, 1994; 1996; 1999; 2001; see also Ward *et al*, 1999). In order to investigate this phenomenon a "Famous faces" test was devised in which subjects were asked to identify a series of photographs of famous and unknown faces. Previous research would suggest that patients with right frontal damage should be more likely to falsely identify the unknown faces.

Twelve black and white photographs were shown to the participants, and in each case they were asked if they recognised the person. If they responded that they did recognise that person, they were asked to give their name and their occupation. Six of the photographs depicted famous faces, who were well-known entertainers, politicians or members of the royal family. The remaining six photographs were of unknown actors, selected to match the style of the famous photographs as closely as possible.

One point was awarded for each correctly identified name and for each correctly identified occupation. If a subject gave an incorrect name, or an incorrect occupation for a famous or unknown face, these were also recorded. These were strictly scored, so that participants who responded "Don't know" or "They look like they might work in..." were not included in this category. Only if the participant gave a confident incorrect response were these recorded. Table 3.23 shows the average number of correctly identified famous names and occupations (out of a maximum of 12), and the number of incorrect responses given in response to both famous and unknown faces.

Table 3.23:
Mean Correct and Incorrect Responses on the Famous Faces Test

	Frontal	Posterior	Control
Valid N	39	14	50
Mean Correct Responses to Famous Faces (Maximum 12)	9.51 (2.43)	8.36 (2.56)	10.31 (1.20)
Mean Incorrect Responses to Famous Faces (Maximum 12)	0.44 (0.72)	0.50 (0.76)	0.26 (0.53)
Mean Incorrect Responses to Unknown Faces (Maximum 12)	0.46 (1.10)	0.07 (0.27)	0.72 (1.25)

One way analysis of variance on correct responses revealed a significant effect of group ($F_{(2, 98)} = 3.35$, $p = 0.039$), with a significant covariate of years of education ($F_{(1, 98)} = 4.33$, $p = 0.04$). Pairwise comparisons confirmed that the control group correctly identified significantly more famous people than the posterior group ($p = 0.015$). The frontal group, however, were not significantly impaired. Analysis at the second level revealed no significant effects (See Appendix 1 ref 2.12).

Analysis of incorrect responses, with Face Type (famous or unknown) as the within subjects factor and Group as the between subjects factor revealed no main effect of Face Type ($F_{(1, 98)} = 0.97$, $p = 0.33$), or of Group ($F_{(2, 98)} = 0.37$, $p = 0.70$). However there was a significant Face Type x Group Interaction ($F_{(2, 98)} = 3.85$, $p = 0.03$), illustrated in Figure 3.1.

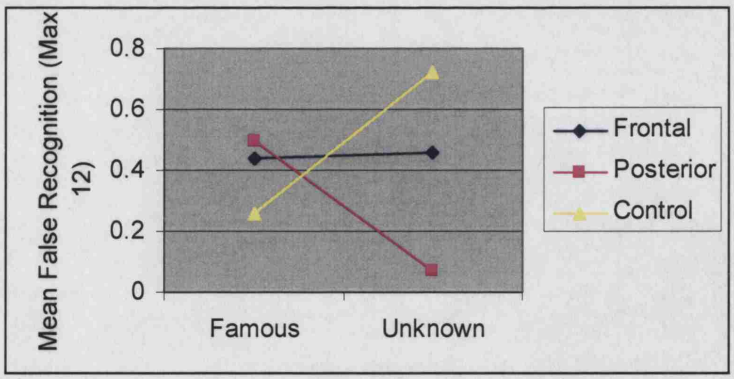


Figure 3.1: False Identification of Famous and Unknown Faces

Despite transformation Levene's test for equality of error variances was significant for both famous ($F_{(2, 100)} = 3.88$, $p = 0.02$), and unknown faces ($F_{(2, 100)} = 10.89$, $p = 0.000$). Therefore this interaction was unpacked using non-parametric tests. Kruskal Wallis tests revealed no significant group differences for famous ($\chi^2 = 2.08$, $df = 2$, $p = 0.35$), or unknown faces ($\chi^2 = 3.63$, $df = 2$, $p = 0.16$). Wilcoxon matched pairs signed ranks tests (to assess whether there were different rates of false recognition to famous and unknown faces within each group) revealed a significant difference within the Control group ($Z = -2.35$, $p = 0.02$), but no differences within the Frontal ($Z = -0.07$, $p = 0.95$) or Posterior ($Z = -1.73$, $p = 0.08$) groups. Analysis at the second level revealed no significant effects (see Appendix 1 ref 2.21).

The lack of a frontal or right frontal effect on false recognition is surprising in light of previous suggestions that frontal patients show elevated rates of false recognition, and that right frontal patients in particular have high rates of false facial recognition. It is possible that with small numbers of stimuli in each condition the present test was not sensitive enough to pick up any existing group differences. (This may also explain why no Frontal or Posterior deficit in true recognition was found, in contrast to the RMT results). However it is interesting that whilst the Control group showed a significantly higher false recognition rate in response to unknown faces (presumably reflecting the lack of knowledge they had about these faces), both the Frontal and Posterior groups had equal false recognition rates in both categories, possibly reflecting a lack of knowledge about the famous faces that led to false responding.

3.3.2 Recall:

Two standardised tests of recall memory ability were administered – one for verbal information (The Story Recall component of the Adult Memory and Information Processing Battery; AMIPB, Coughlan & Hollows, 1985), and one for visual information (The Rey-Osterrieth Complex Figure Test; Rey, 1941; Osterrieth, 1944).

3.3.2.1 Story Recall:

The story recall subtest of the AMIPB was administered as a test of verbal recall. Participants are read a short story and then asked to recall it immediately and after a 30-minute delay. Recall scores and incorrectly recalled ideas (intrusions) are reported, as well as the percentage of information retained over the delay.

Table 3.24:
Story Recall Performance

	Frontal	Posterior	Control
N	40	11	50
Mean Immediate Recall Score / 56	31.75 (13.11)	27.27 (15.54)	38.72 (8.71)
Mean Intrusions in Immediate Recall	0.93 (1.49)	0.27 (0.47)	0.86 (1.20)
Mean Delayed Recall Score / 56	28.40 (13.98)	24.09 (16.50)	35.76 (8.89)
Mean Intrusions in Delayed Recall	1.38 (1.97)	0.45 (0.93)	1.32 (1.28)
Mean Retained Percentage	86.16 (30.52)	73.18 (38.68)	92.44 (11.94)

Analysis of variance revealed a significant effect of group on two of these measures (See Appendix 1 refs 1.7, 1.8, 1.9, 2.14, 2.16, 2.17 for insignificant analyses)

Immediate Recall:

There was a significant effect of group on immediate recall score ($F_{(2, 96)} = 6.85$, $p = 0.002$), with a significant covariate of age ($F_{(1, 96)} = 10.70$, $p = 0.001$). Pairwise comparisons confirmed that the Control group obtained higher delayed recall scores than the Frontal ($p = 0.005$) and Posterior ($p = 0.003$) groups. However further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded no significant differences (see Appendix 1 refs 2.13, 3.8, 4.8, 5.8, 6.8).

Delayed Recall:

There was a significant effect of group on delayed recall score ($F_{(2, 96)} = 7.33$, $p = 0.001$), with a significant covariate of age ($F_{(1, 96)} = 12.70$, $p = 0.001$). Pairwise comparisons confirmed that the Control group achieved significantly higher delayed recall scores than the Frontal ($p = 0.004$) and Posterior ($p = 0.002$) groups. However further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded no significant differences (see Appendix 1 refs 2.15, 3.9, 4.9, 5.9, 6.9).

In summary, our story recall task revealed a Frontal and Posterior deficit in recall of prose information immediately and after a delay, but did not reveal any functional heterogeneity within the frontal lobes in terms of performance on this task. This general frontal deficit in recall is in keeping with previous research (Daum & Mayes, 2000; Dimitrov *et al* 1999; Janowsky *et al*, 1989; Jetter *et al*, 1986; Shimamura *et al*, 1991; Wheeler *et al*, 1995), and has often been attributed to the additional strategic demands placed on memory in recall tasks as opposed to recognition tasks (Moscovitch & Winocur, 2002; Shimamura 2002; Stuss & Benson, 1986). However given the verbal recognition deficit on the RMT we must assume that our Frontal group has a more generalised memory impairment. The fact that our Frontal group did not produce any more intrusions in story recall than our Control group however is somewhat surprising in the light of previous research suggesting that this is often a factor in the recall of Frontal patients (Baldo *et al*, 2002; Daum & Mayes, 2000; Delbecq-Derouesne *et al*, 1990; Mayes & Daum, 1997; Melo *et al*, 1999).

3.3.2.2 Rey-Osterrieth Complex Figure Test (CFT):

The CFT is a frequently used test of visuo-spatial constructional ability and visual memory based on copy and recall of a complex abstract figure. Participants were asked initially to make a copy of the figure, and then were unexpectedly asked to recall as much of the figure as they could after a filled 40-minute delay. In addition to the standard measures of copy time, copy score, and recall score, we adopted the additional scoring systems devised by Bennett-Levy (1984) to assess the strategy adopted at copy, as this has been found to have a significant effect on subsequent recall. His scoring procedure assesses good continuation and symmetry at copy, which together form an overall "strategy" score.

In initial analyses looking at sex differences on all measures within the Control group, we found significant differences in performance between males and females on both CFT copy time and CFT recall score. Therefore we also checked for sex differences in performance on these two measures amongst the Frontal group. Analysis revealed no

significant differences (Copytime: $t_{(23)} = 0.13$, $p = 0.90$; Recall Score: $t_{(31)} = 0.98$, $p = 0.33$). Having ruled out this possible confound we proceeded with the analysis as normal.

Table 3.25:
CFT Performance Data

	Frontal	Posterior	Control
N	29	14	49
Mean Copy Time	228.52 (91.13)	192.14 (79.75)	172.49 (62.85)
N	41	14	49
Mean Copy Score	31.40 (7.26)	31.82 (5.95)	34.04 (2.84)
N	39	14	50
Mean Good Continuation Score / 18	12.51 (3.85)	10.71 (3.56)	12.98 (2.98)
N	39	14	50
Mean Symmetry Score/ 18	7.33 (4.14)	9.29 (5.28)	9.64 (4.53)
N	39	14	50
Mean Strategy Score / 36	19.85 (6.93)	20.00 (6.98)	22.62 (6.46)
N	37	13	48
Mean Delayed Recall Score	12.78 (7.24)	13.85 (6.88)	15.98 (6.20)

Significant group differences were found on four of these measures, discussed in turn below (See Appendix 1 refs 1.10, 1.11, 1.12, 2.18, 2.20 for insignificant analyses).

Copy Time:

Firstly there was a significant effect of group on Copy Time ($F_{(2, 87)} = 4.83$, $p = 0.01$), with a significant covariate of age ($F_{(1, 87)} = 14.67$, $p = 0.000$). Pairwise comparisons confirmed that the Control group were significantly faster in copying the Rey figure than the Frontal group ($p = 0.003$).

Further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.26:
Mean Rey Copy Time: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	7	6	5	7	49
Mean (SD)	208.43 (69.26)	250.83 (142.56)	216.60 (83.29)	262.14 (86.58)	172.49 (62.85)

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(4, 67)} = 2.83$, $p = 0.031$) with a significant covariate of age ($F_{(1, 67)} = 9.53$, $p = 0.003$). Pairwise comparisons confirmed that the Control group had significantly faster copy times then the Medial ($p = 0.021$) and Right Lateral ($p = 0.026$) groups.

Analysis at the third level revealed no further results (see Appendix 1 refs 3.10, 4.10, 5.10, 6.10).

Copy Score:

Although there was no significant effect of group on Rey copy score (see Appendix 1), a significant effect of Frontal Subgroup was found ($F_{(4, 79)} = 3.03$, $p = 0.022$).

Table 3.27:
Mean Rey Copy Score: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	12	8	8	9	49
Mean (SD)	34.83 (1.34)	28.56 (9.60)	33.13 (3.98)	30.44 (7.25)	34.04 (2.84)

Pairwise comparisons confirmed that the Medial group had significantly impaired scores compared to the Control group ($p = 0.004$).

Symmetry Score:

There was also a significant effect of group (Control Frontal or Posterior) on Symmetry Score ($F_{(2, 98)} = 3.17$, $p = 0.046$). However corrected pairwise comparisons revealed no significant group differences, and further exploration yielded no Frontal Subgroup effects (see Appendix 1 ref 2.19).

Delayed Recall:

There was also a significant effect of group (Control, Frontal or Posterior) on delayed recall score ($F_{(2, 93)} = 3.83$, $p = 0.025$), with a significant covariate of age ($F_{(1, 93)} = 26.10$, $p = 0.000$). Pairwise comparisons confirmed that the Control group obtained significantly higher recall scores than the Frontal group ($p = 0.007$).

Further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.28:
Mean Rey Delayed Recall Score: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	12	7	7	7	48
Mean (SD)	14.25 (7.28)	8.43 (6.02)	16.21 (5.08)	12.29 (8.16)	15.98 (6.20)

Analysis of variance revealed a significant effect of Frontal Subgroup ($F_{(,4, 74)} = 4.37$, $p = 0.003$) with a significant covariate of age ($F_{(1, 74)} = 22.46$, $p = 0.000$). Pairwise comparisons confirmed that the Medial group had significantly lower recall scores than the Control group ($p = 0.000$).

Analysis at the third level revealed no further results (see Appendix 1 refs 3.11, 4.11, 5.11, 6.11).

In order to investigate the extent to which the Medial deficit in recall of the figure was due to their poor performance at copy, analysis of the effect of Frontal Subgroup on recall was re-run with the addition of copy score as a covariate. This eliminated the effect of Frontal Subgroup ($F_{(4, 80)} = 1.09$, $p = 0.37$) and showed a highly significant covariate of Copy Score ($F_{(1, 80)} = 15.00$, $p = 0.000$), indicating that the Medial groups poor recall performance was due to their poor Copy performance.

To summarise, we found a marked Medial deficit on the CFT, with impairments on time taken to copy the figure, accuracy in copy, and recall after a 40-minute delay. The Right Lateral group was also slow to copy the figure. We found no Frontal deficit on any of the strategy measures, which was in contrast to previous research which has suggested a frontal impairment in organisation at the copy stage (Lezak, 1995; Lhermitte, Derouesne & Signoret, 1972; Pillon, 1981; Taylor, cited in Kolb & Whishaw, 1985). However the Medial impairment in copy accuracy implies that this group were processing the material less well, even if their strategic approach was within normal limits. The fact that the

Medial effect on recall disappeared when Copy Score was added as a covariate strongly implies that their poor recall performance was due to problems at the encoding stage.

The fact that the most consistently impaired group was the Medial group and not the Right Lateral group may be surprising in light of the prevailing view that visual processing is lateralised to the right hemisphere, and that this group may be most impaired on the CFT (Binder, 1982). Whilst we did find slow performance at copy amongst our Right Lateral patients, we did not find any deficit in accuracy of their copy, or in subsequent recall performance. However this is in keeping with previous reports that the CFT may not reliably distinguish between left and right lateralised brain damage (Barr, Chelune, Hermann, Loring, Perrine, Strauss, Trenarry & Westerveld, 1997; King, 1981; Loring, Lee & Meador, 1988). The reasons for the Medial deficit on the CFT are less obvious. However it is consistent with the results of Diamond *et al* (1997) who reported encoding impairments in a subset of their ACoA patients (who are likely to have suffered medial damage) on the CFT, and Diamond & DeLuca (1996) who also reported poor CFT performance in ACoA amnesics.

3.3.3 Matched Recall and Recognition:

The Doors and People Test (D&P; Baddeley, Emslie & Nimmo-Smith, 1994) was administered as it offers directly comparable measures of recall and recognition, in both the verbal and visual domains. This allows more controlled assessment of the patterns of preserved and impaired memory functions. Table 3.29 shows mean age-scaled scores for performance on each measure for the D&P Test.

Table 3.29:
Doors and People Test Performance

	Frontal	Posterior	Control
N	35	8	49
Mean Overall Age-Scaled Score	8.46 (3.59)	8.88 (2.59)	11.69 (3.18)
N	37	9	49
Mean "People" Age Scaled Score (Verbal Recall)	8.21 (3.51)	7.89 (4.12)	10.98 (3.22)
N	38	10	50
Mean "Doors" Age Scaled Score (Visual Recognition)	8.66 (3.14)	8.30 (2.31)	10.80 (2.83)
N	38	11	50
Mean "Shapes" Age-Scaled Score (Visual Recall)	8.34 (3.97)	11.09 (2.43)	11.36 (2.47)
N	37	9	50
Mean "Names" Age-Scaled Score (Verbal Recognition)	8.84 (3.76)	8.22 (3.96)	11.28 (3.65)

Memory Performance:

Investigation of possible differential deficits in visual vs verbal memory and in recall vs recognition memory was carried out using a 2 x 2 x 3 mixed model ANOVA with Stimulus Type (verbal or visual) and Memory Type (recall or recognition) as the within subjects variables, and Group as the between subject variable. This revealed a significant effect of Group ($F_{(2, 89)} = 12.37$, $p = 0.000$). Pairwise comparisons confirmed that the Frontal group was significantly impaired compared to the Controls ($p = 0.000$). There was no effect of Stimulus Type ($F_{(1, 89)} = 1.80$, $p = 0.18$), nor a Stimulus Type x Group interaction ($F_{(2, 89)} = 8.10$, $p = 0.34$). Neither was there any effect of Memory Type ($F_{(1, 89)} = 0.17$, $p = 0.68$), nor a Memory Type x Group interaction ($F_{(2, 89)} = 0.99$, $p = 0.38$).

Further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.30:
Mean Doors & People Test: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N Mean "People" Age Scaled Score (Verbal Recall)	11 8.81 (3.79)	7 8.57 (4.24)	7 8.57 (3.87)	8 7.75 (2.82)	49 10.98 (3.22)
N Mean "Doors" Age Scaled Score (Visual Recognition)	11 9.82 (2.86)	8 8.00 (2.88)	7 9.14 (3.34)	8 9.00 (2.88)	50 10.80 (2.83)
N Mean "Shapes" Age-Scaled Score (Visual Recall)	11 9.27 (3.93)	8 7.63 (3.34)	7 11.14 (4.14)	8 7.38 (2.97)	50 11.36 (2.47)
N Mean "Names" Age-Scaled Score (Verbal Recognition)	12 10.00 (4.00)	8 9.00 (3.00)	9 8.00 (2.00)	9 10.00 (5.00)	50 11.00 (4.00)

A 2 x 2 x 3 mixed model ANOVA with Stimulus Type (verbal or visual) and Memory Type (recall or recognition) as the within subjects variables, and Frontal Subgroup as the between subject variable revealed a significant effect of Frontal Subgroup ($F_{(4, 75)} = 4.46$, $p = 0.003$). Pairwise comparisons confirmed that all frontal subgroups were impaired compared to the Control group: Orbital ($p = 0.023$), Medial ($p = 0.007$), Left Lateral ($p = 0.044$) and Right Lateral ($p = 0.007$). There was no effect of Stimulus Type ($F_{(1, 75)} = 0.45$, $p = 0.51$), nor a Stimulus Type x Frontal Subgroup interaction ($F_{(4, 75)} = 1.06$, $p = 0.38$). Neither was there any effect of Memory Type ($F_{(1, 75)} = 0.54$, $p = 0.47$), nor a Memory Type x Frontal Subgroup interaction ($F_{(4, 75)} = 1.81$, $p = 0.14$).

Analysis at the third level yielded no significant results (see Appendix 1 refs 3.12-3.15, 4.12-4.15, 5.12-5.15, 6.12-6.15).

Forgetting Measures:

Age scaled forgetting scores were derived for visual and verbal recall according to the scoring instructions provided in Baddeley *et al* (1994), and are presented in Table 3.31. A lower score indicates more forgetting.

Table 3.31:
Verbal and Visual Forgetting Age-Scaled Scores

	Frontal	*Posterior*	Control
N Mean Verbal Forgetting Age-Scaled Score	35 8.28 (2.63)	9 7.70 (2.75)	50 10.34 (2.53)
N Mean Visual Forgetting Age-Scaled Score	37 9.78 (2.04)	10 9.50 (2.27)	50 10.34 (1.89)

A mixed model ANOVA with Stimulus Type (verbal or visual) as the within-subjects measure and Group as the between subjects measure revealed a significant effect of Group ($F_{(2, 89)} = 8.14$, $p = 0.001$). Pairwise comparisons confirmed that both the Frontal ($p = 0.001$) and the Posterior ($p = 0.009$) groups were impaired compared to the Control group. There was no effect of Stimulus Type ($F_{(1, 89)} = 0.54$, $p = 0.46$), but there was a significant Stimulus Type x Group interaction ($F_{(2, 89)} = 3.38$, $p = 0.04$), shown in Figure 3.2 below.

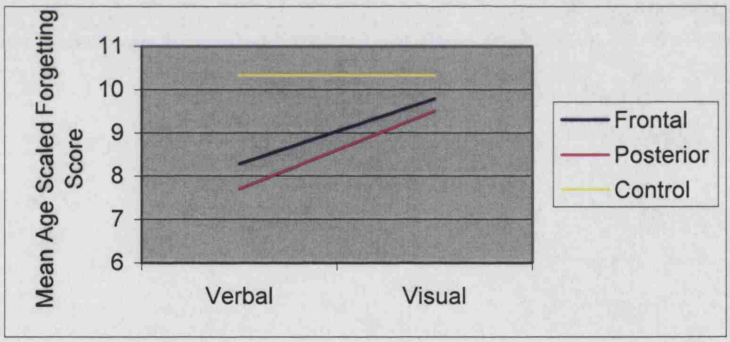


Figure 3.2: Visual and Verbal Forgetting Score by Group

It appears from Figure 3.2 that the group difference in forgetting scores arises from verbal forgetting, in which the Frontal and Posterior groups are much more impaired than visual forgetting. The Control group's forgetting scores are identical for the two stimulus types. Simple main effects analysis confirmed this observation, with one-way analysis of variance revealing a significant effect of Group on verbal forgetting score ($F_{(2, 91)} = 9.13$, $p = 0.000$). Pairwise comparisons confirmed that the Control group obtained significantly

higher verbal forgetting scores than either the Frontal ($p = 0.000$) or Posterior ($p = 0.003$) groups. In contrast there was no effect of Group on visual forgetting scores ($F_{(2, 92)} = 1.46$, $p = 0.24$).

Further exploration of whether this deficit might be specific to particular Frontal Subgroups yielded the following results.

Table 3.32:
Mean Visual and Verbal Forgetting Scores: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N Mean Verbal Forgetting Age-Scaled Score	10 8.10 (2.56)	8 8.38 (2.77)	7 9.00 (2.77)	8 8.12 (2.85)	50 10.34 (2.53)
N Mean Visual Forgetting Age-Scaled Score	9 9.20 (2.62)	8 9.25 (2.76)	7 10.71 (0.76)	8 10.75 (0.71)	50 10.34 (1.89)

A mixed model ANOVA with Stimulus Type (verbal or visual) as the within subjects variable, and Frontal Subgroup as the between subjects variable revealed no significant effect of Stimulus Type ($F_{(1, 75)} = 0.83$, $p = 0.37$), nor a Stimulus Type x Frontal Subgroup interaction ($F_{(4, 75)} = 1.70$, $p = 0.16$). However there was a significant effect of Frontal Subgroup ($F_{(4, 75)} = 3.08$, $p = 0.02$). However Levene's test for equality of error variances was significant for visual forgetting scores ($F_{(4, 77)} = 2.87$, $p = 0.03$). Therefore verbal and visual forgetting scores were analysed separately using one-way ANOVA for verbal forgetting scores, and Kruskal-Wallis for visual scores.

Analysis of variance revealed a significant effect of Frontal Subgroup on verbal forgetting score ($F_{(4, 76)} = 3.00$, $p = 0.023$). Pairwise comparisons confirmed that the Orbital ($p = 0.016$) and Right Lateral ($p = 0.023$) groups were significantly impaired compared to the Controls. However consistent with the level 1 analyses a Kruskal-Wallis test revealed no effect of Frontal Subgroup on visual memory forgetting scores ($\chi^2 = 5.93$, $df = 4$, $p = 0.20$).

Analysis at the third level revealed the following results.

Table 3.33:
Mean Verbal and Visual Forgetting Scores: Grouping / Analysis Level 3

		IMOnly	SMIM	LLat	RLat
Verbal Forgetting Scores	Area Damaged Mean Score (SD)	N = 15 7.00 (1.73)	N = 11 8.54 (2.97)	N = 11 8.81 (2.86)	N = 12 9.00 (2.92)
	Area Not Damaged Mean Score (SD)	N = 19 9.05 (2.88)	N = 23 7.95 (2.47)	N = 23 7.82 (2.50)	N = 19 7.68 (2.37)
Visual Forgetting Scores	Area Damaged Mean Score (SD)	N = 15 9.40 (2.32)	N = 12 9.42 (2.27)	N = 12 10.08 (1.31)	N = 12 10.25 (1.54)
	Area Not Damaged Mean Score (SD)	N = 20 9.95 (1.90)	N = 23 9.87 (2.01)	N = 23 9.52 (2.39)	N = 23 9.43 (2.29)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the Inferior Medial area were significantly impaired in their verbal forgetting compared to those without Inferior Medial damage ($t_{(30.15)} = 2.58$, $p = 0.015$; adjusted degrees of freedom adopted to Control for unequal variance). There were no significant effects on visual forgetting. This finding strongly corroborates the Orbital finding in the level 2 analysis, confirming that those patients with damage in the Inferior Medial region have accelerated forgetting of verbal material on the Doors and People Test.

In summary, the results from the Doors and People Test revealed a general frontal impairment on all memory measures. Each frontal subgroup was impaired compared to the Controls on verbal and visual recall and recognition. There were no interactions that would have indicated differential deficits for different stimulus types or memory measures within the Frontal group. However the forgetting measures revealed that although the Frontal group were not impaired at retaining visual information, they did show a significant impairment at retaining verbal information. Level 2 analyses revealed that the Orbital and Right Lateral groups had significantly accelerated forgetting compared to the Controls. The Orbital finding was corroborated by the level 3 analyses, in which those patients with Inferior Medial damage had significantly accelerated forgetting compared to those without Inferior Medial damage.

3.3.4 Interim Summary: Memory Functioning in the Sample:

Table 3.34:
Patterns of Impairment on Baseline Memory Tasks.

TASK	CRITICAL AREAS (SIGNIFICANTLY IMPAIRED COMPARED TO CONTROLS)
RMT	General Frontal Impairment (no subgroup effects)
FAMOUS FACES	No significant effects
STORY RECALL	General Frontal Impairment (no subgroup effects)
REY	
Copy Time	Medial, Right Lateral
Copy Score	Medial
Delayed Recall	Medial
DOORS AND PEOPLE	
Memory	All Subgroups Impaired
Verbal Forgetting	Orbital, Right Lateral (IMOnly impaired in Level 3 analyses)

Baseline tests of memory function confirmed the presence of memory impairments in the frontal group. Deficits in recognition as well as recall performance, and in verbal as well as visual memory were found. The data therefore suggest a general frontal memory deficit extending to recognition as well as more demanding recall tasks. Only two tests revealed specific subgroup effects. These were in visual recall, where the Medial group were found to have impaired recall of the Rey Complex Figure. This appeared to be due to an encoding deficit at the Copy stage. The other effect was in verbal forgetting, where the Orbital and Right Lateral subgroups appeared to have accelerated forgetting of verbal material in the Doors and People Test. The Orbital result was confirmed by the 3rd level of analysis, which revealed an Inferior Medial accelerated forgetting effect.

In order to assess whether these impairments might reflect a "pure" memory deficit, or a deficit that is secondary to executive problems at encoding or retrieval, critical memory analyses were re-run with the addition of an "Executive Score" as a covariate. This score was produced by calculating z scores for each participant on all critical executive measures. These were Stroop Colour–Word score, Trails B time, FAS words produced, Proverbs score, and TEA sustained attention score. These z scores were summed, and the

resulting "Executive Score" entered into the following critical memory analyses as a covariate[9].

Recognition Memory Test:

The previous mixed model ANOVA with stimulus type (words or faces) as the within subjects variable and Group as the between subjects variable was re-run with Executive Score as a covariate. As before this revealed a significant effect of Group ($F_{(2, 87)} = 5.50$, $p = 0.006$) with both the Frontal ($p = 0.03$) and Posterior ($p = 0.003$) groups having lower recognition scores than the Control group. Executive Score was not a significant covariate ($F_{(1, 87)} = 1.46$, $p = 0.23$). However there was an additional effect of Stimulus Type ($F_{(1, 87)} = 22.34$, $p = 0.000$), with higher recognition scores being obtained for words than faces. There was no Stimulus Type x Group interaction ($F_{(2, 87)} = 0.55$, $p = 0.58$).

Story Recall:

The previous one-way ANOVAs for immediate and delayed recall score were re-run with the addition of Executive Score as a covariate. Analysis of immediate recall revealed that the effect of Group was no longer present ($F_{(2, 87)} = 2.64$, $p = 0.08$). Executive score approached significance as a covariate ($F_{(1, 87)} = 3.74$, $p = 0.056$). Similarly analysis of delayed recall score revealed that the effect of Group was no longer present ($F_{(2, 87)} = 2.96$, $p = 0.06$). However Executive Score was not a significant covariate ($F_{(1, 87)} = 1.92$, $p = 0.17$).

Rey-Osterrieth Complex Figure Test (CFT):

The previous one-way ANOVAs on Copy Time, Copy Score and Delayed Recall Score were re-run with Executive Score as a covariate. In all cases the previously significant effect of Group was eliminated (**Copy Time**: $F_{(2, 74)} = 1.69$, $p = 0.19$; **Copy Score**: $F_{(2, 85)} = 0.08$, $p = 0.93$; **Delayed Recall Score**: $F_{(2, 80)} = 1.06$, $p = 0.35$). However Executive Score did not approach significance as a covariate in any case.

[9] The previous covariates of Age and Years of Education were removed for these analyses

Doors & People:

The previously run mixed model ANOVA with Stimulus Type (visual vs verbal) and Memory Type (recall vs recognition) as the within subjects factors and Group as the between subject factor was re-run with Executive Score as a covariate. In this case a significant effect of group was still present ($F_{(2, 82)} = 5.90$, $p = 0.004$) with the Frontal group having impaired memory performance compared to the Control group ($p = 0.001$). Executive Score was not significant as a covariate ($F_{(1, 82)} = 1.82$, $p = 0.18$).

The previously run one-way ANOVA on verbal forgetting was also re-run with Executive Score as a covariate. Again the significant effect of Group remained ($F_{(2, 83)} = 5.21$, $p = 0.007$). However pairwise comparisons revealed that only the Posterior group was now impaired compared to the Control groups ($p = 0.008$). The Frontal effect was no longer present. Executive Score was not significant as a covariate ($F_{(1, 83)} = 1.59$, $p = 0.21$). (The addition of executive score as a covariate also removed the effect of Frontal Subgroup on verbal forgetting in a one-way ANOVA: $F_{(4, 68)} = 1.31$, $p = 0.28$).

Taking executive performance (as measured by 5 standardised tests) into account eliminated the Frontal memory impairment in Story Recall, all Rey Complex Figure measures, and the Verbal Forgetting measure of the Doors and People Test. It did not eliminate the frontal impairment in performance on the RMT or general memory performance on the Doors & People. However there is at least some evidence that certain memory impairments within the frontal group might be mediated by executive impairments.

3.4 GENERAL CONCLUSIONS:

Baseline assessment of the series with standardised neuropsychological tests has revealed several interesting results. First it has confirmed that there are no language or visual perception problems in the frontal group, excluding these factors as potential explanations for frontal deficits in any other tests. Secondly, the results from standard

tests of executive functioning revealed subgroup effects that have confirmed many previous findings. Most notably no Orbital effects were found on executive tests, whilst Medial, Left Lateral and Right Lateral damage impaired performance. Using acute patients is generally more problematic than using chronic patients, so it is even more convincing that previous findings are being replicated. This suggests that the lesion grouping methodology adopted here is powerful enough to reveal interesting lesion specificity effects. Finally the presence of impairments in several general memory tasks has been confirmed in the frontal group, justifying more detailed investigation of which specific memory processes are impaired following frontal lobe lesions, and whether it might be possible to draw more detailed conclusions about lesion-behaviour relationships in this regard. There is evidence that at least some of these memory impairments might be mediated by executive impairments at either the encoding or retrieval stage.

CHAPTER FOUR:
CONFABULATION BATTERY

4.1 INTRODUCTION

Confabulation has frequently been reported in association with frontal lobe damage following various aetiologies (e.g. Dalla Barba *et al*, 1990; Kern *et al*, 1992; Damasio *et al*, 1985b; Stuss *et al*, 1978, see Chapter 1 for a full discussion). It is reported most frequently in autobiographical or episodic memory recall. However there is evidence that in more rare cases it may also be observed in semantic memory (Baddeley & Wilson, 1986; Delbecq-Derouesne *et al*, 1990; Kopelman *et al*, 1997a; Moscovitch & Melo, 1997).

Dalla Barba and colleagues (Dalla Barba *et al*, 1990; Dalla Barba, 1993a) devised a "confabulation battery" to systematically assess the types of memory probes which elicited confabulation. The battery consisted of 95 questions probing different types of information – personal semantic, general semantic, linguistic semantic, episodic, orientation in time and place, and questions that would elicit an "I don't know" response from normal subjects in both the semantic and episodic domains. In a series of studies using various modifications of this battery they have reported that most patients confabulate only in response to questions probing episodic memory and orientation to time and place (patient CA, Dalla Barba *et al*, 1990; patient MB, Dalla Barba 1993a,b; patient GA, Dalla Barba *et al*, 1997; patient OI, Nedjam *et al*, 2000). However in some more extreme cases confabulations also occurred in response to questions in the semantic domain and to "I don't know" questions (patient SD, Dalla Barba 1993b; patient AB, Kopelman *et al* 1997a; patient BY, Nedjam *et al*, 2000). Although the battery has been used extensively to investigate confabulation in single case investigations, and once in a group study of Alzheimer's patients (Dalla Barba *et al*, 1999) to our knowledge it has never been employed in a frontal series.

To establish whether confabulation was present in our sample, and in what context it occurred, a modified version of Dalla Barba's confabulation battery (Dalla Barba *et al*,

1990; Dalla Barba, 1993a) was administered. This test aims to establish to which questions and under which circumstances confabulation appears.

4.2 METHOD

Questions were selected from Dalla Barba's (1993a) confabulation battery to create a battery of 31 items. This was made up of five questions in each of the following categories: orientation in time (e.g. What month is it?), orientation to place (e.g. Which city are we in?), general semantic memory (e.g. What happened to President Kennedy?), personal semantic memory (e.g. What is your address?), and personal episodic memory (e.g. What did you do yesterday?). In addition five questions which would elicit the answer "I don't know" from most normal participants were included (e.g. Who is the current world fencing champion?), and participants were also asked to tell the story of Red Riding Hood (a mythological question probing semantic memory, see Appendix 2 for full battery). The battery was therefore capable of assessing orientation in time and place, and the presence of confabulation in both episodic and semantic memory.

The questions were put to subjects in a random order, and responses were scored as "correct", "confabulation", or "don't know". For personal semantic memory and personal episodic memory questions, all answers were checked with a relative of the patient, and answers were scored as correct if they matched the information given by the relative. In all other cases there were clear correct answers, and responses were scored by the examiner. In one case (the question "What time is it now?") responses were scored as correct if they fell within two hours (one hour behind and one hour ahead) of the correct time. Answers were only classified as a confabulation if the information given was clearly incorrect. If any subjects gave vague answers they were asked for clarification. Therefore there were no uncertainties about how to classify responses.

4.3 RESULTS

The number of correct, confabulatory and "don't know" responses for each category of question is shown in table 4.1 below.

Table 4.1:
Mean Correct, Confabulatory and "Don't Know" Responses in Confabulation Battery

	Frontal	Posterior	Control
Valid N	38	12	50
Total Confabulations	2.00 (3.00)	0.67 (1.44)	0.58 (0.64)
General Semantic Memory Questions (Maximum 5):			
Mean Correct Responses	4.76 (0.63)	4.75 (0.62)	4.80 (0.49)
Mean "Don't Know" Responses	0.08 (0.27)	0.17 (0.58)	0.10 (0.36)
Mean Confabulations	0.15 (0.49)	0.08 (0.29)	0.10 (0.36)
Personal Semantic Memory Questions (Maximum 5):			
Mean Correct Responses	4.84 (0.44)	4.75 (0.87)	4.98 (0.14)
Mean "Don't Know" Responses	0.00 (0.00)	0.17 (0.58)	0.02 (0.14)
Mean Confabulations	0.13 (0.41)	0.08 (0.29)	0.00 (0.00)
Personal Episodic Memory Questions (Maximum 5):			
Mean Correct Responses	4.42 (1.08)	4.75 (0.62)	5.00 (0.00)
Mean "Don't Know" Responses	0.13 (0.41)	0.17 (0.58)	0.00 (0.00)
Mean Confabulations	0.45 (0.89)	0.08 (0.29)	0.00 (0.00)
Orientation In Time Questions (Maximum 5):			
Mean Correct Responses	4.58 (0.68)	4.75 (0.45)	4.90 (0.36)
Mean "Don't Know" Responses	0.02 (0.16)	0.00 (0.00)	0.00 (0.00)
Mean Confabulations	0.39 (0.68)	0.25 (0.45)	0.10 (0.36)
Orientation in Place Questions (Maximum 5):			
Mean Correct Responses	4.47 (0.89)	4.75 (0.62)	4.80 (0.40)
Mean "Don't Know" Responses	0.08 (0.27)	0.08 (0.29)	0.08 (0.27)
Mean Confabulations	0.45 (0.86)	0.17 (0.58)	0.12 (0.33)
"Don't Know" Questions (Maximum 5):			
Mean Correct Responses	0.16 (0.37)	0.08 (0.29)	0.22 (0.42)
Mean "Don't Know" Responses	4.63 (0.54)	4.92 (0.29)	4.62 (0.49)
Mean Confabulations	0.21 (0.41)	0.00 (0.00)	0.16 (0.37)
Little Red Riding Hood Story (Maximum 1):			
Mean Correct Responses	0.61 (0.50)	0.75 (0.45)	0.74 (0.44)
Mean "Don't Know" Responses	0.16 (0.37)	0.25 (0.45)	0.16 (0.37)
Mean Confabulations	0.23 (0.43)	0.00 (0.00)	0.10 (0.30)

Analysis:

As the control group were frequently at ceiling for correct responses or at floor for errors, (with resulting standard deviations of 0), Kruskal Wallis tests were conducted comparing

the three groups (Frontal, Posterior and Control) with regard to the number of correct and confabulatory responses provided in each category (Don't Know responses were not analysed). Kruskal Wallis tests were also conducted at the second level of analysis (Frontal Subgroup) to look for any specific subgroup effects. As before, level 3 analyses are reported only where a Frontal effect is found at the first analysis level.

Total Confabulations:

Analysis with Kruskal-Wallis revealed a significant effect of Group on the total number of confabulations produced throughout the battery (χ^2 = 10.92, df = 2, p = 0.004). Pairwise Mann-Whitney U comparisons confirmed that the Frontal group produced significantly more confabulations than the Control group (U = 625.50, p = 0.003). The presence of confabulation in the frontal sample was therefore confirmed. There was no sign of excess confabulations in the Posterior group.

Further exploration of whether this deficit might be specific to a particular subset of the frontal group yielded the following results.

Table 4.2
Mean Total Confabulations: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	7	50
Mean (SD)	3.09 (4.57)	1.88 (2.03)	1.25 (1.67)	0.71 (0.76)	0.58 (0.64)

A Kruskal-Wallis test revealed a significant effect of Frontal Subgroup (χ^2 = 12.94 df = 4, p = 0.012), and pairwise Mann-Whitney U comparisons confirmed that both the Orbital (U = 114.00, p = 0.001) and the Medial (U = 120.50, p = 0.049) groups produced significantly more confabulations than the Control group.

Analysis at the third level revealed the following results.

Table 4.3
Mean Total Confabulations: Grouping / Analysis Level 3

	IMonly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 3.00 (3.86)	N = 11 1.81 (2.23)	N = 13 1.77 (2.35)	N = 11 0.72 (0.79)
Area Not Damaged Mean Score (SD)	N = 19 1.21 (1.84)	N = 25 2.16 (3.40)	N = 23 2.22 (3.44)	N = 25 2.64 (3.50)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the Right Lateral region produced significantly fewer confabulations than those without damage to this area ($t_{(28.91)} = 2.59$, $p = 0.02$). This Right Lateral sparing corroborates the level 2 findings above, but there was no significant SMIM or IMonly effect which might have been expected on the basis of the Orbital and Medial effects.

Having confirmed a Frontal effect on total confabulations, more detailed analysis was carried out examining the rates of confabulation within each question type (General Semantic Memory, Personal Semantic Memory, Personal Episodic Memory, Orientation In Time, Orientation in Place, "Don't Know" Questions, and the Little Red Riding Hood Story).

General Semantic Memory:

No significant Group or Frontal Subgroup effects were found (see Appendix 3 refs 1.1, 1.2, 2.1, 2.2)

Personal Semantic Memory:

No significant Group or Frontal Subgroup effects were found (see Appendix 3 refs 1.3, 1.4, 2.3, 2.4).

Personal Episodic Memory:

A Kruskal Wallis test revealed a significant effect of Group on the number of correct responses to personal episodic memory questions ($\chi^2 = 16.02$, df = 2, $p = 0.000$). Pairwise Mann-Whitney U comparisons confirmed that both the Frontal ($U = 675.00$, p =

0.000) and Posterior (U = 250.00, p = 0.004) groups produced significantly fewer correct responses than the Control group.

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group yielded the following results.

Table 4.4:
Mean Correct Responses to Personal Episodic Memory Questions: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	7	50
Mean (SD)	3.91 (1.51)	4.63 (0.74)	4.50 (0.76)	5.00 (0.00)	5.00 (0.00)

A Kruskal Wallis test revealed a significant effect of Frontal Subgroup (χ^2 = 25.70 df = 4, p = 0.012). Pairwise Mann-Whitney U comparisons confirmed that the Orbital (U = 150.00, p = 0.000), Left Lateral (U = 125.00, p = 0.000) and Medial (U = 150.00, p = 0.000) groups all produced significantly fewer correct responses than the Control group.

Analysis at the third level revealed the following results.

Table 4.5:
Mean Correct Responses to Personal Episodic Memory Questions: Grouping / Analysis Level 3

	IMonly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 4.00 (1.32)	N = 11 4.55 (0.93)	N = 13 4.38 (0.96)	N = 11 4.91 (0.30)
Area Not Damaged Mean Score (SD)	N = 19 4.74 (0.73)	N = 25 4.32 (1.18)	N = 23 4.39 (1.20)	N = 25 4.16 (1.25)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the Right Lateral area gave significantly more correct answers to personal episodic memory questions that those without damage to this area ($t_{(29.55)}$ = -2.82, p = 0.008). This confirms the Right Lateral sparing seen in the level 2 analyses. The lack of effects using

IMonly, SMIM and LLat groupings is also consistent with the previous level 2 analysis, in that these groups do not appear to be differentially impaired.

There was also a significant effect of Group on the number of confabulations in response to personal episodic memory questions (χ^2 = 17.20, df = 2, p = 0.000). Pairwise Mann-Whitney U comparisons confirmed that the Frontal group produced significantly more confabulations that the Control group (U = 675.00, p = 0.000).

Further exploration of whether this deficit might be specific to a particular subset of the frontal group yielded the following results.

Table 4.6:
Mean Number Of Confabulations Produced In Response To Personal Episodic Memory Questions: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	7	50
Mean (SD)	0.91 (1.38)	0.25 (0.46)	0.38 (0.52)	0.00 (0.00)	0.00 (0.00)

A Kruskal Wallis test revealed a significant effect of Frontal Subgroup (χ^2 = 25.75 df = 4, p = 0.000), with pairwise Mann-Whitney U comparisons confirming that the Orbital (U = 150.00, p = 0.000), Left Lateral (U = 125.00, p = 0.000) and Medial groups (U = 150.00, p = 0.000) produced significantly more confabulations than the Control group.

Analysis at the third level revealed the following results.

Table 4.7:
Mean Number Of Confabulations Produced In Response To Personal Episodic Memory Questions: Grouping / Analysis Level 3

	IMonly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 0.76 (1.15)	N = 11 0.36 (0.67)	N = 13 0.46 (0.66)	N = 11 0.09 (0.30)
Area Not Damaged Mean Score (SD)	N = 19 0.21 (0.54)	N = 25 0.52 (1.00)	N = 23 0.48 (1.04)	N = 25 0.64 (1.04)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage

to the Right Lateral region produced significantly fewer confabulations in response to personal episodic memory questions that those without damage to this area ($t_{(31.34)}$ = 2.43, p = 0.02). Again this confirmed the Right Lateral sparing seen in the level 2 analysis, and was consistent with the idea that those with Orbital, Left Lateral and Medial damage are equally impaired.

Orientation In Time:

A Kruskal Wallis test revealed a significant effect of Group on the number of correct responses to questions probing orientation to time (χ^2 = 9.21, df = 2, p = 0.01). Pairwise Mann-Whitney U tests confirmed that the Frontal group produced significantly fewer correct responses than the Control group (U = 703.00, p = 0.002).

Further exploration of whether this deficit might be specific to a particular subset of the frontal group yielded the following results.

Table 4.8:
Mean Number Correct Responses To Questions Probing Orientation In Time: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	7	50
Mean (SD)	4.36 (0.92)	4.50 (0.76)	4.88 (0.35)	4.57 (0.53)	4.90 (0.36)

A Kruskal Wallis test revealed a significant effect of Frontal Subgroup (χ^2 = 13.20 df = 4, p = 0.01). Pairwise Mann-Whitney U comparisons confirmed that the Orbital (U = 172.00, p = 0.002), Right Lateral (U = 115.50, p = 0.011) and Medial groups (U = 140.50, p = 0.018) all produced significantly fewer correct responses to questions probing orientation in time than the Control group.

Analysis at the third level revealed the following results.

Table 4.9:
Mean Number Correct Responses To Questions Probing Orientation In Time: Grouping / Analysis Level 3

	IMonly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 4.47 (0.80)	N = 11 4.55 (0.69)	N = 13 4.84 (0.38)	N = 11 4.63 (0.50)
Area Not Damaged Mean Score (SD)	N = 19 4.63 (0.60)	N = 25 4.56 (0.71)	N = 23 4.39 (0.78)	N = 25 4.52 (0.77)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the Left Lateral region gave significantly more correct answers to questions probing orientation in time than those without damage to this area ($t_{(33.41)} = -2.35$, $p = 0.03$). Again this confirmed the Left Lateral sparing seen in the level 2 analysis, and was consistent with the Orbital, Right Lateral or Medial impairments seen.

There was also a significant effect of Group on the number of confabulations produced in response to questions probing orientation to time ($\chi^2 = 7.89$, $df = 2$, $p = 0.019$). Pairwise Mann-Whitney U comparisons confirmed that the Frontal group produced significantly more confabulations than the Control group ($U = 727.50$, $p = 0.005$).

Further exploration of whether this deficit might be specific to a particular subset of the frontal group yielded the following results.

Table 4.10:
Mean Number Confabulations Produced in Response to Questions Probing Orientation in Time: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	7	50
Mean (SD)	0.55 (0.93)	0.50 (0.76)	0.13 (0.35)	0.43 (0.53)	0.01 (0.36)

A Kruskal Wallis test revealed a significant effect of Frontal Subgroup ($\chi^2 = 10.88$ $df = 4$, $p = 0.028$). Pairwise Mann-Whitney U comparisons confirmed that the Orbital ($U = 196.50$, $p = 0.012$), Right Lateral ($U = 115.50$, $p = 0.011$) and Medial ($U = 140.50$, $p =$

0.018) groups produced significantly more confabulations to questions probing orientation in time than the Control group.

Analysis at the third level revealed the following results.

Table 4.11:
Mean Number Confabulations Produced in Response to Questions Probing Orientation in Time: Grouping / Analysis Level 3

	IMonly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 0.47 (0.80)	N = 11 0.45 (0.69)	N = 13 0.15 (0.38)	N = 11 0.36 (0.50)
Area Not Damaged Mean Score (SD)	N = 19 0.37 (0.60)	N = 25 0.40 (0.71)	N = 23 0.57 (0.79)	N = 25 0.44 (0.77)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the Left Lateral region produced significantly fewer confabulations in response to questions probing orientation in time than those without damage to this area ($t_{(33.36)} = 2.12$, $p = 0.04$). Once again this confirmed the Left Lateral sparing seen in the level 2 analysis and was consistent with the undifferentiated impairments seen in the other groups.

Orientation in Place:

Analysis of the number of correct responses and the number of confabulations produced in this category failed to reveal any Group effects (see Appendix 3, refs 1.5, 1.6). However analysis at the second level did reveal the following results for both correct responses and confabulations in response to questions probing orientation to place.

Table 4.12:
Orientation to Place Analyses: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	7	50
Mean Correct Responses (SD)	4.36 (1.21)	4.25 (0.71)	4.63 (0.74)	5.00 (0.00	4.80 (0.40)
Mean Confabulations (SD)	0.55 (1.21)	0.63 (0.74)	0.38 (0.74)	0.00 (0.00)	0.12 (0.33)

A Kruskal Wallis test revealed a significant effect of Frontal Subgroup on correct responses (χ^2 = 10.16 df = 4, p = 0.038). Pairwise Mann-Whitney U comparisons (with a corrected significance level of p = 0.013 in the absence of an initial frontal impairment) confirmed that the Medial group produced significantly fewer correct responses than the Control group in this category (U = 110.00, p = 0.008).

There was also a significant effect of Frontal Subgroup on the number of confabulations produced (χ^2 = 9.60 df = 4, p = 0.048). Pairwise Mann-Whitney U comparisons (again with a corrected significance level of p = 0.013) confirmed that the Medial group produced significantly more confabulations than the Control group (U = 121.00, p = 0.007).

Level 3 analyses are not conducted in this category in the absence of a general Frontal effect.

"Don't Know" Questions:

No significant Group or Frontal Subgroup effects were found (see Appendix 3 refs 1.7, 1.8, 2.5, 2.6).

Little Red Riding Hood Story:

No significant Group or Frontal Subgroup effects were found (see Appendix 3 refs 1.9, 1.10, 2.7, 2.8).

4.4 SUMMARY AND PERFORMANCE-BASED ANALYSIS:

In summary, the confabulation battery has confirmed the presence of confabulation in the Frontal group. Effects were found for questions probing personal episodic memory, in which the Orbital, Medial and Left Lateral groups produced significantly fewer correct responses and significantly more confabulations than Controls. Level 3 analysis confirmed the right lateral sparing in this domain. There were also effects for orientation to time, in which the Orbital, Medial and Right Lateral groups produced significantly fewer correct responses and significantly more confabulations than Controls. Level 3 analysis confirmed the left lateral sparing in this domain. Finally there was an effect for orientation to place, in which the Medial group produced significantly fewer correct responses and significantly more confabulations than the Controls. There were no significant effects for general or personal semantic memory questions, for "I don't know" questions, or for the mythological (Little Red Riding Hood) question.

Performance-Based Analysis

Following the approach of Stuss *et al* (2002) we also examined the presence of confabulation by first selecting patients according to performance, and then examining the sites of their lesions. We looked at those patients who produced a total number of confabulations outside the normal range (i.e. 3 or more confabulatory answers across the battery). There were eight patients who fell into this category, whose lesion locations are shown in table 4.13 below.

Table 4.13:
Lesion location of patients producing total confabulations outside the normal range.

			Level 2 Grouping	Level 3 Grouping			
Patient ID	**Total Confabulations**	**Aetiology**	**Major Lesion Site**	**SMIM damage**	**IMonly damage**	**LLat damage**	**RLat damage**
143	16	ACoA	Orbital	No	Yes	No	No
131	7	ACoA	N/A	Yes	No	Yes	No
108	6	ACoA	Orbital	No	Yes	No	No
106	5	Meningioma	Left Lateral	No	Yes	Yes	No
136	5	Lymphoma	N/A	No	Yes	Yes	No
145	5	ACoA	Medial	No	Yes	No	No
150	5	ACoA	Medial	Yes	No	No	No
110	3	AVM	Orbital	No	Yes	No	No

It is clear from this analysis that every patient who falls outside the normal range in terms of the number of confabulations produced, without exception, has a lesion affecting the inferior medial frontal lobe. Two have additional superior medial damage, and three have additional left lateral damage, but there is no suggestion of any right frontal involvement in this group. A Fisher's Exact test confirmed the significance of the inferior medial region: within the confabulating group 8 (100%) have IM damage; in contrast amongst the non-confabulating patients 18 (62%) have IM damage ($p = 0.04$, one-tailed test). Full details of each patient's lesion are given in table 4.14. This breakdown shows that in six out of the eight cases the inferior medial damage is located in the orbital region, whilst in the other two it is restricted to the anterior cingulate. The results of this performance-led lesion analysis therefore confirm the previous analysis by lesion group in highlighting the orbital and medial regions as critically involved in confabulation.

Table 4.14:
Detailed lesion analysis for confabulating patients.

ID	Total Confabs	LEFT	LEFT					LEFT					
		ORBITAL	MEDIAL					LATERAL					
			Sub Genu	Cingulate		Superior Frontal Gyrus		Superior Frontal Gyrus		Middle Frontal Gyrus		Inferior Frontal Gyrus	
				Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
		IM	IM	IM	IM	SM	SM	L	L	L	L	L	L
143	16	1	0	0	0	0	0	0	0	0	0	0	0
131	7	1	1	1	0	1	0	1	0	0	0	0	0
108	6	1	0	0	0	0	0	0	0	0	0	0	0
106	5	1	0	0	0	0	0	0	0	0	0	1	1
136	5	1	0	0	0	0	0	0	0	0	0	1	1
145	5	0	0	0	0	0	0	0	0	0	0	0	0
150	5	0	0	1	1	0	0	0	0	0	0	0	0
110	3	0	0	0	0	0	0	0	0	0	0	0	0
Sum amongst 8 outside normal range:		5	1	2	1	1	0	1	0	0	0	2	2
Sum amongst 29 within normal range:		10	3	5	3	3	1	7	2	4	4	4	5

ID	Total Confabs	RIGHT	RIGHT					RIGHT					
		ORBITAL	MEDIAL					LATERAL					
			Sub Genu	Cingulate		Superior Frontal Gyrus		Superior Frontal Gyrus		Middle Frontal Gyrus		Inferior Frontal Gyrus	
				Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
		IM	IM	IM	IM	SM	SM	L	L	L	L	L	L
143	16	1	0	0	0	0	0	0	0	0	0	0	0
131	7	1	1	1	0	0	0	0	0	0	0	0	0
108	6	0	0	0	0	0	0	0	0	0	0	0	0
106	5	0	0	0	0	0	0	0	0	0	0	0	0
136	5	0	0	0	0	0	0	0	0	0	0	0	0
145	5	0	0	1	0	0	0	0	0	0	0	0	0
150	5	0	0	1	1	1	0	0	0	0	0	0	0
110	3	1	0	0	0	0	0	0	0	0	0	0	0
Sum amongst 8 outside normal range:		3	1	3	1	1	0	0	0	0	0	0	0
Sum amongst 29 within normal range:		5	1	0	1	3	3	5	5	5	5	4	2

4.5 DISCUSSION

The confabulation battery served as an initial clinical test for the presence of confabulation in our sample, and it has demonstrated convincingly that at least a subset of the patients are confabulating. More specifically, analysis of the types of questions which elicited confabulation bear on several important issues relating to the previous literature. Consistent with the majority of previous reports, we have found no evidence for widespread confabulation in the semantic memory domain, probed using either general semantic or personal semantic questions. Our data therefore support observations using this type of test that confabulation is most common in episodic memory. Consistent with the work of Dalla Barba and colleagues (Dalla Barba *et al*, 1990; 1997; Dalla Barba 1993a,b; Nedjam *et al*, 2000) we found that confabulation was most marked in personal episodic memory, orientation to time, and orientation to place. We also found no evidence that confabulations were elicited in response to "Don't Know" questions. This is consistent with most previous research (Dalla Barba *et al*, 1990, 1997; Dalla Barba, 1993a, but see Fotopolou *et al*, 2004, Mercer *et al*, 1977 and Dalla Barba, 1995, patient SD, for exceptions). Taken together these results indicate that confabulation is not simply the result of filling the gaps created by a faulty memory system[10]. Rather, using this procedure, confabulation seemed to arise in response only to particular categories of information.

Dalla Barba (1993b) has argued that confabulation will be found in the same memory domains that are deficient. Therefore he argues that episodic confabulation will arise in conjunction with impaired episodic memory, whilst semantic confabulation will arise in conjunction with semantic knowledge impairments (see also Baddeley & Wilson, 1986, patient RJ). In contrast with this, Moscovitch & Melo (1997) have argued that the greater incidence of confabulation in the episodic domain reflects the greater demands that recall from episodic memory makes on frontally located memory control processes compared to

[10] It should be noted that in our battery all of the "Don't Know" questions tapped semantic rather than episodic information. Given the greater prevalence of confabulations in the episodic domain the possibility that confabulations would have been elicited in response to "Don't Know" questions if they demanded episodic information cannot be excluded.

recall from semantic memory. They argue that if semantic and episodic memory tasks are equated for the demand placed on strategic retrieval processes, confabulation will occur in both domains. This battery was not designed to investigate in detail the cause of confabulation at the psychological level. Strategic retrieval demands were not explicitly equated, and there was a possible confound of temporality with the semantic / episodic dimension (the personal episodic memory questions all tapped recent events, which might be more susceptible to confabulation than remote memories, Dalla Barba, Mantovan, Cappelletti & Denes, 1998). Our findings at this stage are therefore compatible with both the Dalla Barba (1993b) and Moscovitch & Melo (1997) accounts.

In terms of lesion location, the most striking feature of these results is the consistent association of the Orbital and Medial regions with the production of confabulations. Both subgroups were associated with confabulation in personal episodic memory and orientation to time, the Medial group were also associated with confabulation in orientation to place, and when performance based analysis was conducted it was revealed that all 8 patients who produced a total number of confabulation outside the normal range had a lesion affecting the inferior medial region (either orbital or anterior cingulate).

To our knowledge this is the first time confabulation has been investigated in a general frontal series, and has confirmed previous theorising about the involvement of the orbital and medial areas in the genesis of confabulations. It is consistent with Schnider *et al* (2000) who highlighted the posterior medial orbitofrontal cortex, and Schacter *et al* (1998) and Moscovitch (1995) who both identified the ventromedial area as critical for confabulation. It is also consistent with the high rate of confabulation observed following rupture and repair of ACoA aneurysms, which tend to result in ventromedial and basal forebrain lesions.

One striking difference to emerge already from the series is the complete dissociation in the Orbital group between their tendency to confabulate, and their preservation on the tests of recall and executive functioning presented in the previous chapter. Confabulation in association with preserved performance on tests of executive function has been

reported before (Dalla Barba *et al*, 1990; Delbecq-Derouesne *et al*, 1990; Papagno & Muggia, 1996) and has been used to argue against a critical role of executive dysfunction in confabulation. However these patients clearly do have frontal pathology. It has been suggested that those patients who are unimpaired on tests of executive function may display a milder degree of confabulation than those who are impaired (see DeLuca & Cicerone, 1991; Kapur & Coughlan, 1980; Kopelman, 1987; Shapiro *et al*, 1981; Stuss *et al*, 1978). However the Orbital group in fact produced more confabulations than the Medial group (an average of 3.09 compared to 1.88) so this seems unlikely. Alternatively it may be that in some cases confabulation and performance on the executive tests measured here are reliant on adjacent but distinct brain areas (Moscovitch & Melo, 1997). Whilst the Medial region seems to be involved in both, the Orbital region seems specifically associated with confabulation.

The results obtained relating to the left and right lateral regions were unexpected. Our results suggested a double dissociation between these areas. The Left Lateral group produced fewer correct responses and more confabulations in response to personal episodic memory questions, whilst those with damage to the Right Lateral region were preserved on these measures in the level 3 analyses. In contrast the Right Lateral group produced fewer correct responses and more confabulations in response to orientation to time questions, whilst those with damage to the Left Lateral region were preserved on these measures in the level 3 analyses. The right hemisphere has been highlighted previously in association with confabulation. Burgess *et al* (1996) in a meta-analysis identified right frontal involvement as critical for confabulation and delusional disorders. However this meta-analysis only divided the frontal lobe into left or right hemisphere, no orbital/medial/lateral subdivisions were made. It is possible then that the right hemisphere involvement was in actual fact the right ventromedial region. Indeed Moscovitch (1995) makes this distinction. The lateral results are therefore surprising, but the degree of confabulation in these patients was far less extreme than in the Orbital and Medial groups. In the performance-led analysis none of the confabulating patients had right lateral damage, and in the three who had left lateral damage this was in addition to inferior medial lesions.

One final point is that the confabulations produced in the confabulation battery are of course provoked, not spontaneous confabulations. There is some suggestion in the literature that these types of confabulation may be qualitatively different and reflect different phenomena. However the eight patients identified in the performance-led analysis were in fact clinically confabulating at the time of testing. Of these three recovered as their post-operative confusion abated, two were transferred from the hospital before further research could be undertaken, and one had frontal behavioural difficulties to such a degree that further testing was abandoned. However we were able to follow up the two remaining patients, and a third (who interestingly did not produce an abnormal number of confabulations in the confabulation battery) who had ongoing confabulatory disorders involving frequent, spontaneous and sometimes bizarre confabulations. These patients and the characteristics of their confabulation are discussed further in chapter 9.

CHAPTER FIVE:
ORGANISATION AND MONITORING IN RECALL

5.1 INTRODUCTION

Frontal impairments in memory tests have variously been attributed to problems with organisation of the to-be-remembered material at encoding, organisation at retrieval and monitoring at retrieval. Two tests were designed in an attempt to separate and examine these different aspects of memory control with both visual material (visual scenes) and verbal material (word lists).

In order to examine the efficiency with which patients are able to organize information at encoding, lists of words belonging to one of four semantic categories were presented either blocked together by category, or mixed randomly. Similarly, pictures were presented in which the composite items were either arranged in real-life scenes, or in a random array. If patients with frontal lobe damage have difficulty in subjectively organising material at encoding, they should be disproportionately impaired in recalling items from the randomly organised versions of these tasks (Daum, Schugens, Spieker, Poser, Schoenle & Birbaumer, 1995; Eslinger & Grattan, 1994; Gershberg & Shimamura, 1995; Hirst & Volpe, 1988; Incisa della Rochetta, 1986; Kopelman & Stanhope, 1998). On the basis of imaging evidence any impairments in organisation at encoding might be expected to particularly marked in the Left Lateral group (Fletcher *et al*, 1998a; Savage *et al*, 2001; Wagner *et al*, 2001).

The existence of retrieval deficits following frontal lobe damage may be probed using cueing at recall. Category cues were provided following free recall of the categorised word lists to explore the effects of this manipulation on recall levels. If poor recall performance following frontal lesions is a result of poor organisation at retrieval, patients should show an improvement in recall following this manipulation (e.g. Gershberg & Shimamura, 1995; Hanley *et al*, 1994; Incisa della Rochetta & Milner, 1993, Vilkki *et al*, 1998). This improvement might be expected to be most prominent in the Right Lateral group, on the basis of the HERA model (e.g. Cabeza *et al*, 1997a; Lepage *et al*, 2000;

Tulving *et al*, 1994; Nyberg *et al*, 1996a; Wagner *et al* 1998a, see Chapter 1, section 1.4.1.2)

Another aspect of retrieval frequently highlighted in theories of memory retrieval and confabulation in patients with frontal damage is post-retrieval monitoring. In order to examine this process the visual and verbal recall tasks were designed so that some items appeared in more than one trial. Subjects were asked to monitor their recall by indicating when they had seen items more than once. Evidence from neuroimaging has linked monitoring functions to the right dorsolateral PFC (Fletcher *et al*, 1996, 1998b; Henson *et al*, 1999b, 2000; Shallice, 2001), so it might be expected that the Right Lateral group will show the greatest impairments here.

The occurrence of intrusions in visual and verbal memory paradigms has been linked to confabulation. It may be that patients with frontal lobe lesions as a group are more likely to make intrusion errors than normal controls, or it may be that abnormally high levels of intrusions are specifically associated with spontaneous confabulation. The experimental tests were therefore designed to provoke and investigate the rates of intrusions in two ways. Firstly, in order to explore intrusions of semantically related but non-presented items in the word list learning task, the key associate from each semantic category was omitted from the lists (e.g. the word "dog" was not presented for the category "animals"). This type of manipulation has been shown to induce false recall, or "extra-list intrusions" in normal and clinical samples (Melo *et al*, 1999; Roediger & McDermott, 1995). Secondly, in order to explore intrusions of previously relevant but now irrelevant items, the word lists and visual scenes were constructed in such a way that the same category of items would be presented for recall in more than one trial, but whilst some of the items within that category had been previously presented, others were new. This manipulation was intended to increase confusion between trials, and lead to the occurrence of "prior-list intrusions", the incorrect recall of items that appeared in previous trials but not the current one.

Visual and verbal versions of this task were developed in order to investigate possible left / right frontal effects. Some investigators have reported disproportionate deficits in memory for verbal materials associated with left frontal damage, and for visual material associated with right frontal damage (Curran *et al*, 1997; Hanley *et al*, 1994; Milner *et al*, 1991; Schacter *et al*, 1996). Imaging results have been mixed, either suggesting that lateralisation is modality specific (Brewer *et al*, 1998; Golby *et al*, 2001; Kelley *et al*, 1998; Lee *et al*, 2000, 2002, Wagner *et al*, 1998b) or that left frontal damage will result in a disproportionate deficit in encoding processes, and right frontal damage will result in a disproportionate deficit in retrieval processes, regardless of stimulus type (e.g. Nyberg *et al*, 1996a; Shallice *et al*, 1994; Tulving *et al*, 1994, see Fletcher & Henson, 2001, for a review).

5.2 METHOD

5.2.1 Verbal Organisation and Monitoring Test (Verbal OM):

Stimuli:

6 lists of 16 words were presented on a computer screen. Each list comprised four words from four different categories, drawn from the Battig & Montague (1969) norms. In each case the prime associate from each category was excluded, and the second, third, fourth and fifth most frequent associates were used to construct the lists.

The words in the first, third and fifth lists were presented in a blocked fashion, such that the words comprising each category were presented together. The words in the second, fourth and sixth lists were randomly intermixed so that although they were still drawn from four categories, subjects would have to organise them into categories themselves to aid recall.

In the first list, each of the four categories were necessarily new. However in lists 2-6, two of the categories were new, whilst two of the categories had already been used in a

previous list. Within these repeated categories, two of the four words were new, and two had already been presented in a previous list. The six word lists can be seen in Appendix 4.

Procedure:

Each word appeared individually in the centre of the computer screen for a duration of 2 seconds, with a further 1 second interval before the next word was presented. Following the last word of each list, subjects were prompted by an on-screen message to add one to a series of random numbers (between 1 and 99) that appeared on the computer screen, and report their answer out loud. This distractor task lasted for 30 seconds, after which subjects were prompted to freely recall as many words from the list as they could remember. They reported these words out loud to the examiner who recorded all responses. Subjects were asked to try to remember as many words as they could with no help, but after they had freely recalled as many words as possible, they were prompted to press a key for "clues". When they did this the names of each of the four categories that comprised that list appeared individually on the computer screen for 20 seconds, to prompt further recall. If the subject recalled any further words, they reported these out loud and they were again recorded by the experimenter.

Following cued recall, the same procedure was repeated for the remaining lists: presentation, distractor task, free recall and cued recall. The lists were presented in the same order in each trial, and the words within each list also remained in a constant order. In lists 2-6 subjects were not only prompted to recall as many words as they could, but also to complete a concurrent monitoring task in which they had to indicate when they had seen any of the words previously in one of the other lists.

5.2.2 Visual Organisation and Monitoring Test (Visual OM):

The visual organisation and monitoring test was designed as a visual analogue of the verbal organisation and monitoring test described above, and is based upon the work of Mandler and colleagues on memory for real world scenes versus unorganised collections

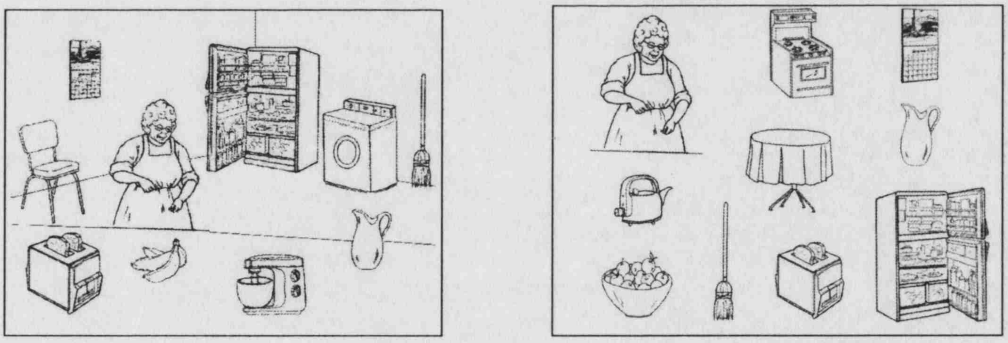
of the same objects (Mandler & Johnson, 1976; Mandler & Parker, 1976; Mandler & Stein, 1974).

Stimuli:

Each subject saw eight scenes, each comprising 10 objects, on the computer screen. Four of the scenes were farm scenes, and four were kitchen scenes. In each of the scenes, 6 of the objects were present in all four pictures, whilst four were present in one only. Pictures were taken from either the Snodgrass & Vanderwart (1980) norms, the British Picture Vocabulary Scale, or were drawn specifically for the task.

In the organised versions, a naturalistic scene was created by arranging the objects in a realistic way, and perspective lines were added to create a coherent whole. In the unorganised versions, perspective lines were removed, and the objects were placed in a random array (see figure 5.1 for examples).

Figure 5.1: Examples of organised and unorganised kitchen scenes.



Each subject saw either four organised farm scenes and four unorganised kitchen scenes, or four organised kitchen scenes and four unorganised farm scenes. Altogether there were four possible sets of eight scenes – two in which the farm scenes were organised and two in which the kitchen scenes were organised, and two possible presentation orders for each one. In each case, presentation of the farm and kitchen scenes were alternated. The number of times each order was used was balanced across participants.

Procedure:

Each scene was presented for 10 seconds on the computer screen, and subjects were instructed to look carefully and try to remember as many items as possible from that scene. Following this subjects were required to add one to a series of random numbers (between 1 and 99) that appeared on the computer screen, and report their answer out loud. This distractor task lasted for 30 seconds, after which subjects were prompted by an on screen message to recall as many items from the picture as they could remember. They reported these items out loud to the examiner who recorded all responses.

The same procedure was repeated for each scene: presentation, distractor task, and free recall. However for scenes 3-8 subjects were not only prompted to recall as many items as they could, but also to complete a concurrent monitoring task in which they had to indicate when they had seen any of the items previously in one of the other scenes.

The Verbal and Visual OM tasks therefore measured several aspects of memory function:

i) The effects of externally provided versus subjective organisation at encoding.

ii) The rates of "extra list intrusions" – words or images which were never presented but were semantically related to the presented words or images

iii) The rates of "prior list intrusions" – items which were presented in an earlier trial but not in the one being currently recalled (the presence of prior list intrusions was made more likely by the fact that although categories or scenes were repeatedly presented, only some of the items within these categories were repeated, and some were new)

iv) Subjects' ability to monitor their memories at retrieval, and accurately identify which items had previously been presented.

v) The effects of prompting at recall (Verbal OM task only).

5.3 RESULTS:

5.3.1 Verbal OM Task

Mean recall performance in free recall on the Verbal OM task is presented in table 5.1.

Table 5.1:
Verbal OM Task: Mean Free Recall Performance

	Frontal	Posterior	Control
N	37	10	50
Mean Correct Recalls per list (Max 16)	6.97 (3.53)	8.32 (3.61)	9.84 (2.59)
Blocked Lists	7.32 (3.81)	9.23 (3.78)	10.44 (2.38)
Random Lists	6.48 (3.45)	7.40 (3.55)	9.25 (3.11)

Correct Recall

Correct recalls were analysed using a mixed model ANOVA with list organisation (Blocked or Random) as the within subjects factor, and Group (Frontal, Posterior or Control) as the between-subjects factor. There was no effect of List Organisation ($F_{(1, 92)} = 0.37$, $p = 0.55$), but there was a significant main effect of Group ($F_{(2, 92)} = 10.85$, $p = 0.000$), with a significant covariate of age ($F_{(1, 92)} = 11.71$, $p = 0.001$). Pairwise comparisons revealed that the Frontal group had significantly lower recall rates than the Control group ($p = 0.000$). There was no significant List Organisation x Group interaction ($F_{(2, 92)} = 1.31$, $p = 0.28$).

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group revealed the following results.

Table 5.2:
Verbal OM Task: Mean Correct Free Recall: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	7	8	7	50
Mean Correct Recalls per list (Max 16)	7.74 (4.22)	6.44 (2.71)	7.71 (4.40)	7.19 (1.75)	9.84 (2.59)
Blocked Lists	8.24 (4.50)	6.00 (2.65)	8.50 (4.80)	7.48 (1.79)	10.44 (2.38)
Random Lists	7.24 (4.06)	5.90 (2.55)	6.92 (4.10)	6.90 (2.34)	9.25 (3.11)

An ANOVA with List Organisation as the within-subjects variable and Frontal Subgroup as the between-subjects variable revealed no significant effect of List Organisation ($F_{(1, 76)} = 0.37$, $p = 0.55$), but there was a significant main effect of Frontal Subgroup ($F_{(4, 76)} = 5.38$, $p = 0.001$), with a significant covariate of age ($F_{(1, 76)} = 12.37$, $p = 0.001$). Levene's test for equality of error variances was significant for both blocked recall ($F_{(4, 78)} = 6.62$, $p = 0.000$), and random recall ($F_{(4, 78)} = 5.69$, $p = 0.000$). However a subsequent Kruskal-Wallis test using combined blocked and random recall rates confirmed the significance of the group difference ($\chi^2 = 13.15$ df = 4, $p = 0.011$). Pairwise Mann-Whitney U comparisons confirmed that both the Medial group ($U = 69.00$, $p = 0.002$) and the Right Lateral group ($U = 73.00$, $p = 0.011$) had significantly poorer recall performance than the Control group. There was no significant List Organisation x Group interaction ($F_{(4, 78)} = 0.82$, $p = 0.52$).

Analysis at the third level revealed no significant results (see Appendix 5, refs 3.1, 4.1, 5.1, 6.1).

Number of Categories Recalled:

Table 5.3:
Verbal OM Task: Mean Number Categories Recalled Per List.

	Frontal	Posterior	Control
N	38	10	50
Mean No. Categories Recalled per List (Max 4)	2.82 (1.00)	3.08 (0.98)	3.57 (0.38)
Blocked Lists	2.82 (0.99)	3.10 (0.92)	3.57 (0.43)
Random Lists	2.82 (1.07)	3.07 (1.10)	3.57 (0.43)

In order to investigate whether reduced recall rates amongst the Frontal group were due to the omission of entire categories, analysis of the mean number of correct categories recalled per list was conducted (only correct free recall performance was included, incorrect intruded categories and any categories recalled following prompting were omitted). A mixed model ANOVA with list organisation (Blocked or Random) as the within subjects factor, and Group (Frontal, Posterior or Control) as the between-subjects factor revealed no effect of List Organisation ($F_{(1, 93)} = 3.17$, $p = 0.08$), but there was a

significant main effect of Group ($F_{(2, 93)} = 13.59$, $p = 0.000$), with a significant covariate of age ($F_{(1, 93)} = 14.38$, $p = 0.000$). Levene's test for equality of error variances was significant for both blocked ($F_{(2, 95)} = 6.17$, $p = 0.003$) and random ($F_{(2, 95)} = 11.94$, $p = 0.000$) lists. However a Kruskal Wallis test using combined blocked and random category recall confirmed the group difference ($\chi^2 = 16.77$, df = 2, $p = 0.000$). Pairwise Mann Whitney U comparisons revealed that the Frontal group recalled significantly fewer categories than the Control group ($U = 472.50$, $p = 0.000$). There was no significant List Organisation x Group interaction ($F_{(2, 93)} = 0.03$, $p = 0.97$).

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group revealed the following results.

Table 5.4:
Verbal OM Task: Mean No. Categories Recalled Per List: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	8	8	7	50
Mean No. Categories Recalled Per List (Max 4)	2.98 (1.07)	2.81 (0.81)	2.92 (1.12)	2.95 (0.42)	3.57 (0.38)
Blocked Lists	2.91 (1.17)	2.79 (0.73)	3.04 (0.97)	2.95 (0.56)	3.57 (0.43)
Random Lists	3.06 (0.98)	2.83 (0.93)	2.79 (1.34)	2.95 (0.45)	3.57 (0.43)

An ANOVA with List Organisation as the within-subjects variable and Frontal Subgroup as the between-subjects variable revealed no significant effect of List Organisation ($F_{(1, 77)} = 2.61$, $p = 0.11$), but there was a significant main effect of Frontal Subgroup ($F_{(4, 77)} = 6.71$, $p = 0.000$), with a significant covariate of age ($F_{(1, 77)} = 13.43$, $p = 0.000$). Levene's test for equality of error variances was significant for both blocked ($F_{(4, 79)} = 4.88$, $p = 0.001$), and random recall ($F_{(4, 79)} = 10.21$, $p = 0.000$). However a subsequent Kruskal-Wallis test using combined blocked and random category recall confirmed the significance of the group difference ($\chi^2 = 15.63$ df = 4, $p = 0.004$). Pairwise Mann-Whitney U comparisons confirmed that both the Medial group ($U = 79.00$, $p = 0.005$) and the Right Lateral group ($U = 42.50$, $p = 0.001$) recalled significantly fewer categories than the Control group. Note however that the absolute level of performance in all four subgroups is very similar. The results here are likely to be due to the smaller standard

deviations in the Right Lateral and Medial groups. There was no significant List Organisation x Group interaction ($F_{(4, 77)} = 0.82$, $p = 0.52$).

Analysis at the third level revealed the following results.

Table 5.5:
Verbal OM Task: Mean No. Categories Recalled Per List: Grouping / Analysis Level 3

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 2.50 (1.16)	N = 11 2.89 (0.95)	N = 13 2.71 (1.31)	N = 11 3.13 (0.49)
Area Not Damaged Mean Score (SD)	N = 19 2.98 (0.75)	N = 25 2.69 (1.01)	N = 23 2.78 (0.78)	N = 25 2.59 (1.10)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the right lateral region recalled significantly more categories per list than those without damage to this region ($t_{(33.97)} = -2.07$, $p = 0.05$). This result is at first surprising as it contradicts the Level 2 result which indicated that the Right Lateral group recalled *fewer* categories than Controls. However as noted before the Right Lateral group actually had a very similar absolute level of performance to the other Frontal subgroups in level 2 analysis, and the significant results in that group was due to the low standard deviation compared to other subgroups. The different grouping methods may also be responsible for these apparently contradictory results. In level 3 analysis those with Right Lateral damage are being compared to all other patients, including the Medial patients who were most impaired on recall of categories, and it is likely that this is driving the effect.

Table 5.6:
Verbal OM Task: Correct Recalls per Category

	Frontal	Posterior	Control
N	35	9	50
Mean No Words Recalled per Category (Max 4)	2.40 (0.52)	2.69 (0.59)	2.73 (0.54)
Blocked Lists	2.56 (0.58)	2.91 (0.68)	2.92 (0.49)
Random Lists	2.25 (0.58)	2.36 (0.60)	2.55 (0.68)

To investigate whether some groups might have poor recall of categories but good recall within each one, the number of words recalled per category was analysed (see table 5.6). As before only correct free recall performance was used in this measure, incorrect intruded categories and any categories recalled following prompting were omitted. A mixed model ANOVA with list organisation (Blocked or Random) as the within subjects factor, and Group (Frontal, Posterior or Control) as the between-subjects factor revealed no effect of List Organisation ($F_{(1,89)} = 0.06$, $p = 0.81$), but there was a significant main effect of Group ($F_{(2, 89)} = 4.39$, $p = 0.02$). Pairwise comparisons revealed that the Frontal group had significantly lower recall per category than the Control group ($p = 0.004$). There was no significant List Organisation x Group interaction ($F_{(2, 89)} = 2.50$, $p = 0.09$).

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group revealed the following results.

Table 5.7:
Verbal OM Task: Correct Recalls per Category: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	10	8	7	7	50
Correct Recalls per Category (Max 4)	2.50 (0.62)	2.22 (0.45)	2.55 (0.73)	2.41 (0.28)	2.73 (0.54)
Blocked Lists	2.73 (0.59)	2.22 (0.52)	2.75 (0.79)	2.50 (0.26)	2.92 (0.49)
Random Lists	2.26 (0.69)	2.22 (0.51)	2.34 (0.72)	2.33 (0.53)	2.55 (0.68)

A mixed model ANOVA with List Organisation as the within-subjects variable and Frontal Subgroup as the between-subjects variable revealed no significant effect of List Organisation ($F_{(1, 75)} = 0.13$, $p = 0.72$), but there was a significant main effect of Frontal Subgroup ($F_{(4, 75)} = 2.59$, $p = 0.04$), with significant covariates of age ($F_{(1, 75)} = 4.55$, $p = 0.04$) and years of education ($F_{(1, 75)} = 5.57$, $p = 0.02$). Pairwise comparisons confirmed that the Medial group recalled significantly fewer words per category than the Control group ($p = 0.005$). There was no significant List Organisation x Frontal Subgroup interaction ($F_{(4, 75)} = 1.40$, $p = 0.24$).

Analysis at the third level revealed no significant results (see Appendix 5 refs, 3.2, 4.2, 5.2, 6.2).

Category Organisation at Recall:

Table 5.8:
Verbal OM Task: Unnecessary Category Switches in Recall

	Frontal	Posterior	Control
N	38	10	50
Mean No. Unnecessary Category Switches per List	0.41 (0.53)	0.68 (0.57)	0.55 (0.44)
Blocked Lists	0.25 (0.51)	0.40 (0.56)	0.36 (0.39)
Random Lists	0.57 (0.67)	0.97 (0.91)	0.74 (0.69)

In order to investigate whether the recall of each group respected category organisation, the number of unnecessary additional category switches made in the recall of each list was recorded. This was calculated by the formula:

No. Category Switches Made – (No. Categories Recalled – 1)

A mixed model ANOVA with list organisation (Blocked or Random) as the within subjects factor, and Group (Frontal, Posterior or Control) as the between-subjects factor revealed no significant effects (**List Organisation:** $F_{(1, 93)} = 0.82$, $p = 0.37$, **Group**: $F_{(2, 93)} = 1.78$, $p = 0.18$, **List Organisation x Group interaction**: $F_{(2, 93)} = 0.48$, $p = 0.62$). Analysis at Level 2 also failed to reveal any significant effects (see Appendix 5, ref 2.3).

Intrusions:

The rates of prior-list and extra-list intrusions produced by each group are presented in table 5.9 below.

Table 5.9:
Verbal OM Task: Mean Intrusion Rates

	Frontal	Posterior	Control
Mean Extra-List Intrusions per list	0.47 (0.49)	1.02 (2.02)	0.36 (0.41)
Blocked Lists	0.63 (0.68)	1.10 (2.11)	0.50 (0.71)
Random Lists	0.31 (0.40)	0.93 (1.95)	0.23 (0.30)
Mean Prior-list Intrusions per list	0.60 (0.75)	0.68 (0.88)	0.60 (0.59)
Blocked Lists	0.77 (1.22)	0.55 (0.86)	0.73 (0.84)
Random Lists	0.49 (0.58)	0.77 (0.94)	0.51 (0.68)

Intrusions were analysed using a mixed model ANOVA with List Organisation (Blocked or Random) and Intrusion Type (Extra-List or Prior-List) as the within subjects factors, and Group (Frontal, Posterior or Control) as the between-subjects factor. There was no main effect of Intrusion Type ($F_{(1, 92)} = 0.15$, $p = 0.64$), List Organisation ($F_{(1, 92)} = 0.34$, $p = 0.56$), or Group ($F_{(2, 92)} = 0.73$, $p = 0.49$). There were also no significant interactions (see Appendix 5 ref 1.1). Analysis at grouping level 2 also failed to reveal any significant differences (see Appendix 5 ref 2.1).

Effects of Prompting on Recall:

Table 5.10 presents the rates of additional recall obtained after the category prompts were given.

Table 5.10:
Verbal OM Task: Mean Recall Performance Following Prompting

	Frontal	Posterior	Control
N	38	10	50
Mean Additional Correct Responses Following Prompting	2.21 (1.50)	1.83 (1.66)	1.45 (0.89)
Blocked Lists	2.35 (1.76)	1.70 (1.78)	1.44 (1.17)
Random Lists	2.09 (1.57)	1.97 (1.91)	1.47 (1.16)
Mean Additional Extra-List Intrusions Following Prompting	0.85 (1.43)	0.95 (1.31)	0.25 (0.30)
Blocked Lists	0.94 (1.56)	0.87 (1.31)	0.24 (0.36)
Random Lists	0.79 (1.44)	1.03 (1.43)	0.26 (0.45)
Mean Additional Prior-list intrusions Following Prompting	0.33 (0.42)	0.22 (0.27)	0.12 (0.20)
Blocked Lists	0.34 (0.47)	0.30 (0.42)	0.10 (0.25)
Random Lists	0.32 (0.52)	0.17 (0.32)	0.13 (0.26)

Correct Recall

Correct recalls following prompting were analysed using a mixed model ANOVA with list organisation (Blocked or Random) as the within subjects factor, and Group (Frontal, Posterior or Control) as the between-subjects factor. There was no effect of List Organisation ($F_{(1, 92)} = 0.87$, $p = 0.35$), or Group ($F_{(2, 92)} = 2.77$, $p = 0.07$), and there was no significant List Organisation x Group interaction ($F_{(2, 92)} = 0.25$, $p = 0.78$).

However analysis at the second level revealed the following results.

Table 5.11:
Verbal OM Task: Mean Correct Recall Following Prompting: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	7	8	7	50
Mean Additional Correct Recalls Following Prompting	1.97 (1.80)	2.25 (0.88)	1.52 (1.12)	2.86 (1.13)	1.45 (0.89)
Blocked Lists	2.06 (2.14)	2.29 (1.22)	1.58 (1.81)	3.29 (1.27)	1.44 (1.17)
Random Lists	1.88 (1.54)	2.29 (1.06)	1.46 (0.96)	2.43 (1.45)	1.47 (1.16)

An ANOVA with List Organisation as the within-subjects variable and Frontal Subgroup as the between-subjects variable revealed no significant effect of List Organisation ($F_{(1, 76)} = 1.45$, $p = 0.23$), but there was a significant main effect of Frontal Subgroup ($F_{(4, 76)} = 2.85$, $p = 0.03$), with a significant covariate of age ($F_{(1, 76)} = 10.13$, $p = 0.002$). Levene's test for equality of error variances was significant for additional recall in the blocked lists ($F_{(4, 78)} = 5.01$, $p = 0.001$). However a subsequent Kruskal-Wallis test confirmed the significance of the group difference with blocked and random lists combined ($\chi^2 = 11.34$ df = 4, $p = 0.023$). Pairwise Mann-Whitney U comparisons were conducted with a corrected significance level of $p < 0.013$ in the absence of a significant level 1 group effect. This confirmed that the Right Lateral group produced significantly more correct recalls following category prompting than the Control group ($p = 0.003$). There was no significant List Organisation x Subgroup interaction ($F_{(4, 78)} = 0.46$, $p = 0.76$).

Intrusions:

Additional intrusions produced following prompting were analysed using a mixed model ANOVA with List Organisation (Blocked or Random) and Intrusion Type (Extra-List or Prior-List) as the within subjects factors, and Group (Frontal, Posterior or Control) as the between-subjects factor. This revealed a significant main effect of List Organisation ($F_{(1, 92)} = 6.91$, $p = 0.01$), with more intrusions being produced following prompting in the blocked lists than the random lists. It also revealed a significant main effect of Group ($F_{(2, 92)} = 8.70$, $p = 0.000$), with pairwise comparisons revealing that both the Frontal group ($p = 0.000$) and the Posterior group ($p = 0.014$) produced a greater number of intrusions than the Control group. There was no effect of Intrusion Type ($F_{(1, 92)} = 0.28$, $p = 0.60$).

There was however a significant Intrusion Type x Group interaction ($F_{(2, 92)} = 3.31$, $p = 0.04$), which is illustrated in figure 5.2.

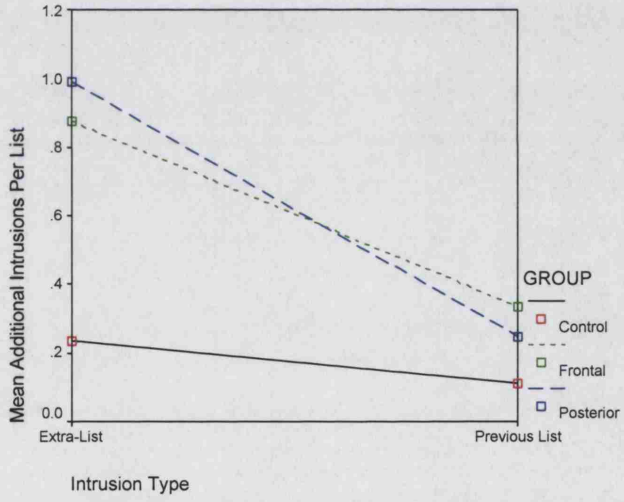


Figure 5.2: Mean Additional Intrusions Produced Following Prompting

Simple main effects analysis was carried out by analysing rates of extra-list intrusions and prior-list intrusions separately with Frontal Subgroup as the between subjects factor. As error variances were unequal in both cases analysis was conducted using non-parametric tests. For extra-list intrusions a Kruskal Wallis test found a significant effect

of Group (χ^2 = 7.51, df = 2, p = 0.02). Pairwise Mann Whitney U comparisons revealed that only the Frontal and Control groups differed significantly from each other (U = 640.00, p = 0.008). There was also a significant effect of Group on prior-list intrusions (χ^2 = 9.19, df = 2, p = 0.01). Pairwise Mann Whitney U comparisons revealed again that only the Frontal and Control groups differed significantly (U = 620.00, p = 0.002). However the lack of a Posterior effect is likely to be due to the small sample size of this group. Although Figure 5.2 indicates that the interaction is due to the Frontal and Posterior groups producing a far greater number of extra-list intrusions that the Control group following prompting, simple main effects analysis cannot support this.

Further exploration of whether these deficits might be specific to a particular subset of the Frontal group yielded the following results.

Table 5.12:
Verbal OM Task: Mean Intrusions Following Prompting: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	11	7	8	7	50
Mean Additional Extra-List Intrusions Following Prompting	1.08 (1.43)	0.71 (0.52)	0.44 (0.72)	0.29 (0.21)	0.25 (0.30)
Blocked Lists	1.18 (1.79)	0.95 (0.78)	0.50 (0.78)	0.19 (0.33)	0.24 (0.36)
Random Lists	0.97 (1.29)	0.57 (0.50)	0.38 (0.68)	0.38 (0.40)	0.26 (0.45)
Mean Additional Prior-list intrusions Following Prompting	0.40 (0.59)	0.28 (0.18)	0.13 (0.15)	0.34 (0.41)	0.12 (0.20)
Blocked Lists	0.36 (0.55)	0.36 (0.38)	0.06 (0.18)	0.36 (0.48)	0.10 (0.25)
Random Lists	0.42 (0.70)	0.19 (0.38)	0.17 (0.25)	0.33 (0.43)	0.13 (0.26)

A mixed model ANOVA with List Organisation (Blocked or Random) and Intrusion Type (Extra-List or Prior-List) as the within-subjects factors, and Frontal Subgroup as the between-subjects factor revealed no significant effect of List Organisation ($F_{(1, 76)} = 0.71$, p = 0.40), or of Intrusion Type ($F_{(1, 76)} = 2.56$, p = 0.11). However there was a significant main effect of Frontal Subgroup ($F_{(4, 76)} = 5.44$, p = 0.001). Pairwise comparisons revealed that the Orbital (p = 0.000) and Medial (p = 0.018) groups both produced significantly more intrusions following prompting than the Control group.

There was also a significant Intrusion Type x Frontal Subgroup interaction ($F_{(4, 76)} = 4.18$, p = 0.04), which is illustrated in figure 5.3.

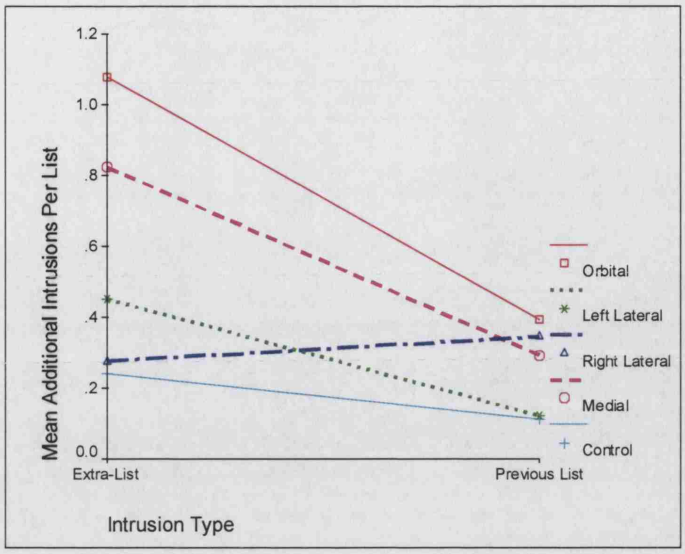


Figure 5.3: Mean Additional Intrusions Produced Following Prompting Grouping / Analysis Level 2

Simple main effects analysis was carried out by analysing rates of extra-list intrusions and prior-list intrusions separately with Frontal Subgroup as the between subjects factor. As error variances were unequal in both cases analysis was conducted using non-parametric tests. For extra-list intrusions a Kruskal Wallis test found only a trend towards a Frontal Subgroup effect ($\chi^2 = 8.99$, $p = 0.06$). However there was a significant effect of Frontal Subgroup on prior-list intrusions ($\chi^2 = 9.54$, $p = 0.05$). Pairwise Mann Whitney U comparisons confirmed that the only group to differ significantly from the Control group was the Right Lateral group, who produced significantly more prior list intrusions following prompting than the Controls ($p = 0.009$). In contrast to the general Frontal effect (where rates of extra-list intrusions were higher than rates of prior-list intrusions) the Right Lateral group show identical rates of extra-list intrusions to the Controls, but have an elevated prior list intrusion rate.

Analysis at the third level was conducted for average additional extra-list intrusions, average additional prior-list intrusions and average additional intrusions combined.

Table 5.13:
Mean Average Additional Intrusions Produced Following Prompting: Grouping / Analysis Type 3

	IMOnly	SMIM	LLat	RLat
Area Damaged	N = 17	N = 11	N = 13	N = 11
Mean Additional Intrusions (SD)	1.42 (1.55)	1.49 (2.52)	1.26 (2.40)	0.69 (0.50)
Extra-List	1.06 (1.17)	1.15 (2.17)	0.99 (2.05)	0.35 (0.27)
Prior-List	0.36 (0.48)	0.35 (0.42)	0.28 (0.40)	0.35 (0.35)
Area Not Damaged	N = 19	N = 25	N = 23	N = 25
Mean Additional Intrusions (SD)	1.09 (1.97)	1.14 (1.36)	1.24 (1.35)	1.49 (2.06)
Extra-List	0.75 (1.69)	0.79 (1.04)	0.85 (1.03)	1.14 (1.69)
Prior-List	0.34 (0.39)	0.35 (0.44)	0.39 (0.45)	0.35 (0.47)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed only one significant difference. In keeping with the interaction found in the level 2 analysis above, those patients with damage to the Right Lateral region were found to produce significantly fewer extra-list intrusions than those without damage to this area ($t_{(26.72)} = 2.28$, $p = 0.03$).

Monitoring:

Table 5.14 shows the mean percentage of repeated words that were correctly identified as repeated by the participants. It also shows the mean percentage of words that were new that were incorrectly identified as repeated (false alarms).

Table 5.14:
Verbal OM Task: Monitoring Performance

	Frontal	Posterior	Control
Percentage Words Correctly Monitored	89.20 % (11.81)	81.67 % (9.53)	88.78 % (10.42)
Percentage Words Incorrectly Identified as Repeated	7.31 % (9.41)	13.95 % (17.98)	5.00 % (9.41)

One-way ANOVAs revealed no significant effect of group on either correct monitoring ($F_{(2, 92)} = 2.64$, $p = 0.08$), or on incorrect monitoring ($F_{(2, 80)} = 2.27$, $p = 0.11$). However it is interesting that the group who tend toward monitoring failures is the Posterior rather

than the Frontal group. The Frontal group, in contrast, are behaving almost exactly like the Controls.

Analysis at the level of Frontal Subgroup also revealed no significant monitoring effects (see Appendix 5 ref 2.2).

Comparison of the recall rates as participants progressed through the test (lists 1 and 2 compared to lists 3 and 4 compared to lists 5 and 6) were also conducted but no theoretically interesting effects were obtained.

Verbal OM Task Summary

Analysis of the verbal OM task revealed that the Frontal group were impaired on free recall of presented words. Level 2 analysis revealed that the Medial and the Right Lateral groups had significantly lower recall than the Controls. Further exploration of the reasons for this reduction in recall revealed that the Frontal group (and again the Medial and Right Lateral groups at Level 2) were recalling fewer categories than Controls. However the mean level of performance indicated that all subgroups were equally impaired compared to Controls and that the lack of significance in the other two subgroups was likely to be due to increased variances. Indeed level 3 analysis showed that those patients with damage to the Right Lateral region actually recalled *more* categories than those without damage to this region. Overall, the Medial group were most severely impaired on both raw recall and number of categories recalled, and this was corroborated by the finding that they also produced fewer words per category in their recall than the Control group. There were no effects regarding unnecessary switching of categories in recall, which would have indicated disorganisation at retrieval. Neither was there any increase in intrusion rates in free recall amongst the Frontal group.

Although providing category cues to aid recall did not yield a general Frontal effect, it did seem to disproportionately help the Right Lateral group whose rates of correct recall following prompting were significantly higher than the Controls. There was however a clear Frontal effect of prompting on the rate of intrusions, with the Orbital and Medial

groups in particular producing significantly more intrusions than the Control group following prompting. Interactions here showed that the Frontal and Control groups produced more extra-list than prior-list intrusions. However the Right Lateral group showed a different pattern, with significantly higher rates of prior-list intrusions following prompting than the Controls, with equal rates of extra-list intrusions. Analysis at the third level supported this, revealing that those patients with damage to the right lateral region produced significantly fewer extra-list intrusions following prompting than those without right lateral damage. This pattern of results implies that prompting at recall induced an uncontrolled responding strategy in the Orbital and Medial groups, who produced more non-presented words (extra-list intrusions) but did not produce any more presented words (correct recalls or prior-list intrusions). In contrast prompting seemed to induce a more controlled responding strategy in the Right Lateral group, who were able to use category prompts to increase their levels of veridical recall whilst controlling non-presented intrusions. The fact that the errors that they did produce were previously presented words rather than extra-list intrusions provides further support for this hypothesis.

Providing organisation at encoding did not have any effect on any measure except on additional intrusions following prompting, when more intrusions were observed for the blocked lists than the random lists. Contrary to expectation, the Frontal group did not show any impairment in their ability to correctly monitor repeated items in their recall. Finally it is noteworthy that the Left Lateral group, who might have been expected to be impaired on the verbal task, were not impaired on any measure.

5.3.2 Visual OM Task

Mean recall performance on the Visual OM task is presented in table 5.15.

Table 5.15:
Visual OM Task: Mean Recall Performance

	Frontal	Posterior	Control
N	40	14	50
Mean Correct Recalls per Picture (Max 10)	5.47 (1.62)	5.37 (2.01)	6.66 (1.07)
Organised Pictures	5.89 (1.87)	5.79 (2.40)	6.89 (1.24)
Random Pictures	5.05 (1.66)	4.95 (1.79)	6.43 (1.11)
Mean Extra-Picture Intrusions per Picture	0.17 (0.27)	0.17 (0.20)	0.06 (0.10)
Organised Pictures	0.14 (0.31)	0.14 (0.19)	0.08 (0.13)
Random Pictures	0.20 (0.31)	0.20 (0.36)	0.05 (0.13)
Mean Prior-Picture Intrusions per Picture	0.52 (0.43)	0.67 (0.62)	0.39 (0.35)
Organised Pictures	0.51 (0.56)	0.71 (0.74)	0.43 (0.42)
Random Pictures	0.51 (0.55)	0.62 (0.66)	0.32 (0.40)

Correct Recall

Correct recalls were analysed using a mixed model ANOVA with Picture Organisation (Organised or Random) as the within-subjects factor, and Group (Frontal, Posterior or Control) as the between-subjects factor. There was no effect of Picture Organisation ($F_{(1, 99)} = 1.92$, $p = 0.17$), but there was a significant main effect of Group ($F_{(2, 99)} = 9.94$, $p = 0.000$), with a significant covariate of age ($F_{(1, 99)} = 20.83$, $p = 0.000$). Levene's test for equality of error variances was significant for recall in the organised pictures ($F_{(2, 101)} = 6.98$, $p = 0.001$). However a subsequent Kruskal-Wallis test on recall in the organised and random pictures combined confirmed the significance of the group difference ($\chi^2 = 14.43$, $df = 2$, $p = 0.001$). Pairwise Mann-Whitney U comparisons confirmed that the Frontal group ($U = 551.00$, $p = 0.000$) produced significantly fewer correct recalls than the Control group. There was no significant Picture Organisation x Group interaction ($F_{(2, 99)} = 1.25$, $p = 0.29$).

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group revealed the following results.

Table 5.16:
Visual OM Task: Mean Correct Recall: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	12	8	9	7	50
Mean Correct Recalls per Picture (Max 10)	6.11 (1.76)	4.56 (1.29)	5.81 (1.61)	5.68 (0.68)	6.66 (1.07)
Organised Pictures	6.71 (2.13)	4.84 (1.45)	6.33 (1.93)	5.86 (0.80)	6.89 (1.24)
Random Pictures	5.52 (1.73)	4.31 (1.48)	5.28 (1.78)	5.50 (0.68)	6.43 (1.11)

An ANOVA with Picture Organisation as the within-subjects variable and Frontal Subgroup as the between-subjects variable revealed no significant effect of Picture Organisation ($F_{(1, 79)} = 1.21$, $p = 0.27$), but there was a significant main effect of Frontal Subgroup ($F_{(4, 79)} = 6.85$, $p = 0.000$), with a significant covariate of age ($F_{(1, 79)} = 13.14$, $p = 0.001$). Levene's test for equality of error variances was significant for organised recall ($F_{(4, 81)} = 4.47$, $p = 0.003$), and random recall ($F_{(4, 81)} = 3.51$, $p = 0.011$). However a subsequent Kruskal-Wallis test using combined organised and random recall rates confirmed the significance of the group difference ($\chi^2 = 16.19$ df = 4, $p = 0.003$). Pairwise Mann-Whitney U comparisons confirmed that both the Medial group ($U = 41.00$, $p = 0.000$) and the Right Lateral group ($U = 77.00$, $p = 0.015$) had significantly poorer recall performance than the Control group. There was no significant Picture Organisation x Group interaction ($F_{(4, 79)} = 1.46$, $p = 0.22$).

Analysis at the third level revealed no significant results (see Appendix 6 refs 3.1, 4.1, 5.1, 6.1).

Intrusions:

Intrusions were analysed using a mixed model ANOVA with Picture Organisation (Organised or Random) and Intrusion Type (Extra-Picture or Prior-Picture) as the within-subjects factors, and Group (Frontal, Posterior or Control) as the between-subjects factor.

There was no main effect of Picture Organisation ($F_{(1, 99)} = 0.94$, $p = 0.33$). However there was an effect of Intrusion Type ($F_{(1, 99)} = 51.32$, $p = 0.000$), with far higher rates of prior-picture than extra-picture intrusions. There was also a main effect of Group ($F_{(2, 99)} = 6.01$, $p = 0.003$). Pairwise comparisons revealed that both the Frontal group ($p = 0.006$) and the Posterior group ($p = 0.006$) produced significantly more intrusions than the Control group. There were no significant interactions (see Appendix 6 ref 1.1).

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group revealed the following results.

Table 5.17:
Visual OM Task: Mean Intrusions: Grouping / Analysis Level 2

	Orbital	Medial	Left Lateral	Right Lateral	Control
N	12	8	9	7	50
Mean Extra-Picture Intrusions	0.22 (0.42)	0.19 (0.27)	0.17 (0.15)	0.07 (0.10)	0.06 (0.10)
Organised Pictures	0.19 (0.51)	0.13 (0.13)	0.08 (0.25)	0.07 (0.12)	0.08 (0.13)
Random Pictures	0.25 (0.35)	0.25 (0.44)	0.25 (0.28)	0.07 (0.12)	0.05 (0.13)
Mean Prior-Picture Intrusions	0.56 (0.45)	0.63 (0.55)	0.52 (0.49)	0.45 (0.33)	0.39 (0.35)
Organised Pictures	0.49 (0.51)	0.49 (0.57)	0.59 (0.66)	0.62 (0.71)	0.43 (0.42)
Random Pictures	0.57 (0.43)	0.72 (0.95)	0.41 (0.49)	0.29 (0.23)	0.32 (0.40)

A mixed model ANOVA with Picture Organisation (Organised or Random) and Intrusion Type (Extra-List or Prior-List) as the within-subjects factors, and Frontal Subgroup as the between-subjects factor revealed no significant effect of Picture Organisation ($F_{(1, 79)} = 0.37$, $p = 0.54$), but there was a significant effect of Intrusion Type ($F_{(1, 79)} = 47.69$, $p = 0.000$), with far more Prior-Picture than Extra-Picture Intrusions being produced. There was also a significant effect of Frontal Subgroup ($F_{(4, 79)} = 2.91$, $p = 0.027$). Pairwise comparisons revealed that the Orbital ($p = 0.022$) and Medial ($p = 0.014$) groups both produced significantly more intrusions than the Control group. There were no significant interactions (see Appendix 6 ref 2.1).

Analysis at the third level revealed no significant differences (see Appendix 6 refs 3.2, 3.3, 4.2, 4.3, 5.2, 5.3, 6.2, 6.3)

Monitoring

Table 5.18 shows the mean percentage of repeated images that were correctly identified as repeated by the participants. It also shows the mean percentage of images that were new that were incorrectly identified as repeated (false alarms).

Table 5.18:
Visual OM Task: Monitoring Performance

	Frontal	Posterior	Control
Percentage Images Correctly Monitored	92.89 % (8.57)	85.99 % (21.92)	94.54 % (5.17)
Percentage Images Incorrectly Identified as Repeated	10.96 % (15.11)	10. 00% (15.61)	7.88% (9.68)

One-way ANOVAs revealed no significant effect of Group on either correct monitoring ($F_{(2, 99)} = 0.57$, $p = 0.57$), or on incorrect monitoring ($F_{(2, 61)} = 0.51$, $p = 0.61$). Once again the data do not provide any evidence for a frontal impairment in monitoring.

Analysis at the level of Frontal Subgroup also revealed no significant monitoring effects (see Appendix 6 ref 2.2).

Visual OM Task Summary

Analysis of the visual OM task revealed that the Frontal group were impaired on free recall of pictures. This deficit seemed to be specific to the Medial and to a lesser extent the Right Lateral group. The Frontal group also produced significantly more intrusions in their recall, and this effect seemed to be specific to the Orbital and Medial subgroups. Far more prior-list than extra-list intrusions were elicited by this paradigm. No frontal impairment in monitoring was found.

5.4 DISCUSSION

Correct Recall:

The results from the verbal and visual versions of the OM task are remarkably consistent. Both revealed a frontal deficit in recall of information. Recall deficits in frontal patients have been reported many times before (Daum & Mayes, 2000; Dimitrov *et al*, 1999; Janowsky *et al*, 1989; Jetter *et al*, 1986; Shimamura *et al*, 1991), indeed Wheeler *et al* (1995) reported that 80% of studies in their meta-analysis had reported some deficit in free recall among patients with frontal lesions. On a more detailed anatomical analysis significant deficits in recall with respect to Controls were obtained in the Medial and Right Lateral groups only. Although not frequently reported (see discussion below), this finding is consistent with a recent report by Alexander *et al* (2003) who found posterior medial and posterior right dorsolateral impairments (amongst others), and with Vilkki *et al* (1998) who found a right anterior impairment (as well as a left anterior impairment) in verbal recall tasks.

Traditional wisdom about the modality specificity of the left and right hemisphere might have suggested that we should find a Right Lateral deficit for recall in the visual OM task, and a Left Lateral deficit in the verbal OM task. However the presence of a Right Lateral deficit in both suggests that a common strategic process is responsible. The HERA model would predict that right frontal damage would disrupt retrieval rather than encoding processes (Nyberg *et al*, 1996a; Shallice *et al*, 1994; Tulving *et al*, 1994). It is possible therefore that our results reflect the existence of two functionally distinct deficits arising from different regions of damage within the prefrontal cortex. It may be that the Medial deficit reflects a "pure" memory deficit arising from disruption of projections from the ventromedial frontal cortex to the medial temporal lobe limbic system[11]. This is supported by the finding that the Medial group recalled significantly fewer categories, and significantly fewer words per category, than the Controls. The Right Lateral deficit on the other hand may reflect a strategy or "executive" deficit at retrieval rather than an

[11] Alternatively this may reflect a deficit in "energising" schemata, or a lack of cognitive effort amongst the medial group (see Stuss, Shallice, Alexander & Picton, 1995)

organic amnesia. This possibility is supported by the performance of this group when category prompts were given to aid recall, and is explored further below.

The Medial and Right Lateral findings are slightly surprising in the light of previous evidence which has tended to find either a general frontal or a predominantly left lateral impairment in recall tasks (e.g. Alexander *et al*, 2003; Dimitrov *et al*, 1999; Incisa della Rochetta & Milner, 1993; Stuss *et al*, 1994, Vilkki *et al*, 1998). There are several reasons why this might be the case. In the Incisa della Rochetta & Milner (1993) and Vilkki *et al* (1998) studies patients were only grouped by hemisphere, so the medial patients in these studies were incorporated into the lateral groups. Similarly in the Dimitrov *et al* (1999) study, some left lateral patients had additional medial damage. Indeed they also reported medial deficits in free recall. These studies may be consistent therefore with our Medial reduction in recall. Turning to the Alexander *et al* (2003) and Stuss *et al* (1994) studies, one reason for the difference in results may be that their procedures involved repeated presentation of the same list, whilst the current procedure involved only one presentation (this also applies to Incisa della Rochetta & Milner 1993, and Vilkki *et al*, 1998). It may be therefore that their results reflect a learning deficit rather than a memory deficit. Both Alexander *et al* (2003) and Stuss *et al* (1994) also concluded that the underlying reason for the recall impairments in their left lateral group might be a mild language impairment as reflected by performance on the Boston Naming Test. The data presented in chapter 3 indicated that our Left Frontal group had no language impairments of this type, as measured by the GNT. This might go some way to explaining the lack of left frontal effects on verbal recall in the present study. However, two of the eight patients in our Left Lateral group actually performed 2 standard deviations below control performance on recall in the Verbal OM task, so it would be dangerous to accept the null hypothesis that there is no Left Lateral effect at all. Instead differences between these studies are most likely to reflect the small group sizes and heterogeneity of lesion sites that result when an overall Frontal group is split into subgroups.

Organisation at Encoding:

Results from both the verbal and visual OM tasks suggest that the provision of externally

provided organization at encoding conferred no recall advantage on any group compared to presenting information randomly. In fact the only measure that was affected by organization at encoding was the production of additional intrusions following prompting, when more intrusions were observed for the blocked lists than the random lists. Our results therefore do not provide any evidence of an encoding deficit in our Frontal group. If these patients had difficulty in subjectively organizing material at encoding then we would have expected an improvement in their recall rates when external organization was provided.

This is in contrast to previous research which has suggested that recall deficits in patients with frontal lesions may be at least in part due to a failure to organize material at encoding (Daum *et al*; 1995, Eslinger & Grattan, 1994; Gershberg & Shimamura, 1995; Hirst & Volpe, 1988; Incisa della Rochetta, 1986; Kopelman & Stanhope, 1998). It is consistent however with the results of Incisa della Rochetta & Milner (1993) who found, contrary to their expectation, that random as opposed to blocked presentation did not result in impairments in recall. Hanley *et al* (1994) also reported that the free recall deficit in their ACoA patient ROB was not aided by providing instructions at study. It is also broadly in keeping with the results of Alexander *et al* (2003), Kopelman & Stanhope (1998) and Stuss *et al* (1994). Although each of these studies reported an increase in recall following organization at encoding in both frontal and control groups (an effect we did not find with our procedure), there was no disproportionate benefit to their frontal patients and therefore no evidence of an encoding deficit in this group.

Organisation at Retrieval:

Analysis of category clustering in recall in the Verbal OM task revealed no evidence that Frontal patients or any Frontal Subgroup were switching category in their recall any more than the Control group. Therefore there is no evidence for general disorganisation of recall amongst the Frontal group. However providing category cues to prompt further recall did yield some interesting effects. Although it did not yield a general Frontal effect, it did have a significant effect on the Right Lateral group. In free recall this group produced significantly fewer correct recalls than Controls. However following prompting

their rate of correct recall was significantly higher than the Controls. This is consistent with Alexander *et al*'s (2003) finding that their right posterior dorsolateral frontal group were significantly impaired at subjective organisation in recall, as it indicates that this group were unable to subjectively organise their recall until external cues were provided. It also provides further evidence that the fundamental deficit in the Right Lateral group is at the retrieval stage, and is consistent with imaging evidence linking the right PFC to retrieval processes (e.g. Cabeza *et al*, 1997a; Lepage *et al*, 2000; Tulving *et al*, 1994; Nyberg *et al*, 1996a; Wagner *et al* 1998a). This facilitatory effect of providing cues at retrieval to patients with frontal lobe damage has been reported many times previously (e.g. Dimitrov *et al*, 1999; Gershberg & Shimamura, 1995; Hanley *et al*, 1994; Incisa della Rochetta & Milner, 1993) and implies that recall cues may trigger a faulty retrieval process. Although it has not previously been reported specifically with right frontal patients, the results reported by Incisa della Rochetta & Milner (1993) do actually show a similar right frontal effect. Their data indicate an average advantage of prompting of about 9.5 words a list for their right frontal group by comparison with 3 words per list for controls. The left frontal group were in between with an advantage of 6 words a list. The same right frontal effect does therefore seem to have been present in previous research, but has not been specifically highlighted.

Intrusions:

Under free recall conditions we found different patterns of intrusions in our verbal and visual paradigms. In the verbal OM task there was no difference in the number of intrusions produced by Frontal, Posterior or Control patients. This seems surprising in the light of several reports concluding that a key feature of recall in frontal patients is the high rate of intrusions (Baldo *et al*, 2002; Daum & Mayes, 2000; Delbecq-Derouesne *et al*, 2990; Melo *et al*, 1999) but it is consistent with Alexander *et al* (2003), Dimitrov *et al*, 1999, Jetter *et al* (1986) and Stuss *et al* (1994) who did not find significantly higher rates of intrusions in their frontal groups compared to controls on word list learning paradigms. However in the visual OM task the Frontal group did produce significantly more intrusions in their recall, and this effect seemed to be specific to the Orbital and Medial subgroups. Similarly there was an effect of prompting in the verbal OM task with

the Frontal group producing significantly more intrusions than the Control group. More detailed analysis once again revealed this to be due to the Orbital and Medial subgroups. Interactions here implied that this was due to a tendency to produce more extra-list than prior-list intrusions, presumably because prompting with a category cue led to the production of more semantically related albeit incorrect responses.

The presence of higher levels of intrusions in the Orbital and Medial frontal groups is strongly reminiscent of the higher rates of confabulation found in these groups with the confabulation battery (Chapter 4). Although intrusions and confabulations are distinct phenomena, intrusions might be seen to reflect a failure to inhibit inappropriate responses and have frequently been considered a confabulatory-like behaviour and used as an approximate measure of confabulation in frontal samples. The present results imply that they may also have common anatomical substrates. The finding that the Posterior group also produced significantly higher rates of intrusions than the Controls on the same two measures was slightly surprising, as this one of the few occasions where a result has been found that is not specifically frontal. It is interesting that the Posterior group includes a number of patients with temporal lobe damage, known to impair memory. The Medial and Orbital frontal groups involve damage to the ventromedial PFC, which has been proposed to be a major component of a limbo-thalamic circuit underlying memory (Bachevalier & Mishkin, 1986; Petrides, 1989) and damage to this region may occur in conjunction with damage to the basal forebrain and cholinergic system involved in memory (Broks *et al*, 19988; Butters, 1985; Easton & Parker, 2003; Gold, 2003; Hasselmo, 1995; Irle & Markowitsch, 1987; Sarter *et al*, 2001, 2003; Thiel, 2003; Whitehouse *et al*, 1981, 1983). Thus a deficit in core memory processes may be involved in the production of intrusions in free recall.

The elicitation of extra-list intrusions with prompting however did not occur in the Right Lateral group. Instead the Right Lateral group produced significantly higher rates of *prior-list* intrusions. The fact that prompting induced higher levels of correct recalls and prior-list intrusions (as opposed to extra-list intrusions) in this group strongly supports the hypothesis that they had a strategic retrieval deficit that was aided by the provision of

category prompts at retrieval. This cueing did not produce undisciplined recall of unpresented words (as it did in the Orbital and Medial groups), but instead enabled them to produce more veridical recalls, with the unfortunate side effect of increased levels of prior-list intrusions (which are much more difficult to reject as incorrect than extra-list intrusions). This may be a result of impaired monitoring processes which have been linked to the right dorsolateral PFC (Fletcher *et al*, 1996, 1998b; Henson *et al*, 1999b, 2000; Shallice, 2001).

Monitoring:

No frontal impairment of monitoring was found in either the verbal or visual OM task. This is surprising in the light of studies that have linked the right dorsolateral region to monitoring functions (Curran *et al*, 2001; Fletcher *et al*, 1996, 1998b; Henson *et al*, 1999b, 2000; Shallice, 2001; Stuss *et al*, 1994). However it is possible that the current procedure either was not sensitive enough to monitoring deficits, or that it was tapping a different monitoring function to those previously associated with frontal lesions. In the study reported by Stuss *et al* (1994) the right frontal impairment was in intra-list repetitions, and the imaging studies concerned tasks such as distinguishing lures from targets (Curran *et al*, 2001), semantic relatedness (Fletcher *et al*, 1996), keeping track of free recall (Fletcher *et al*, 1998b) and source memory (Henson *et al*, 1999b). The monitoring task in the present experiment was slightly different, and may have involved a frequency or temporal component in monitoring whether words had additionally been presented in a previous list, so may involve different processes to those previously studied.

Overall Conclusions:

The visual and verbal OM tasks revealed several interesting anatomically specific memory effects. There was some evidence that the Frontal impairment in recall was driven by two distinct subgroups. The Medial subgroup's recall impairment was not affected by manipulations at encoding or retrieval and may therefore reflect a pure memory deficit arising from disruption of projections from the ventromedial frontal

cortex to the medial temporal lobe limbic system. The Right Lateral subgroup's impairment on the other hand may reflect a strategy or "executive" deficit at retrieval rather than an organic amnesia, which may be overcome by the provision of category cues to aid retrieval. Both the Orbital and Medial subgroups had inflated intrusion rates in these tasks, which may potentially be linked to confabulation.

CHAPTER SIX:
ENCODING SPECIFICITY

6.1 INTRODUCTION

Activation of the left prefrontal cortex has been consistently reported in imaging studies investigating memory encoding (Fletcher *et al*, 1995; Grady *et al*, 1998; Haxby *et al*, 1996; Kapur *et al*, 1994; Nyberg *et al*, 1996a; Shallice *et al*, 1994; Tulving *et al*, 1994). In particular activation of the left ventrolateral pre-frontal cortex (VLPFC), and specifically the left inferior frontal gyrus, has been associated with encoding tasks requiring use of semantic knowledge, in "deep" or elaborated encoding tasks (Dobbins *et al*, 2002; Gabrieli *et al*, 1996, Wig *et al*, 2004), and activation of this region at study is then associated with subsequent recognition accompanied with high confidence (Wagner *et al*, 1998c) or "remember" judgements (Henson *et al*, 1999a). This region has therefore been argued to subserve retrieval and use of semantic knowledge in higher level encoding processes (Demb *et al*, 1995; Tulving *et al*, 1994)

However Thompson-Schill *et al* (1997) proposed a slightly different explanation for the activation of the left IFG in semantic retrieval tasks. In their imaging task they varied the amount of selection required between competing aspects of semantic information necessary to make a match, and found that left IFG activation was dependent on selection demand. They argue that activation of the left IFG is the result not of semantic retrieval *per se* but of the need to select some relevant feature of semantic knowledge from a set of competing alternatives. This "selection" account has also received some support from other studies (Dolan & Fletcher, 1997; Fletcher *et al*, 2000; Thompson-Schill *et al* 1999)

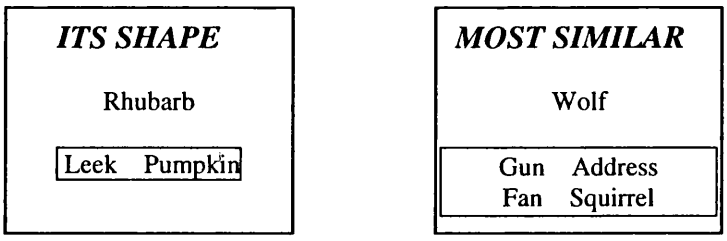
To investigate whether this neuroimaging finding could be supported by neuropsychological investigation with patients, we developed a task closely modelled on Thompson-Schill *et al*'s (1997) "Comparison" task. Subjects were asked to choose words that matched a target word according to either a specific dimension of the word, or on the basis of global similarity. Global similarity judgements do not require selection amongst semantic information so according to Thompson-Schill *et al* (1997) should not involve

the left IFG. The Specific Dimension condition however requires selection of the relevant piece of semantic information from several available alternatives, and should therefore involve the left IFG. In a modification of the original procedure we also included a subsequent memory test, in which subjects were presented with the target word, and required to recall the word that they had chosen to match it. This allows some examination of whether any recall deficits in our Frontal group might be due to difficulties at the encoding stage. Specifically, if those with left IFG damage are unable to carry out elaborated encoding by selecting amongst competing semantic information, then they should show a recall deficit in this condition that is explained by performance at encoding.

6.2 METHOD:

The encoding specificity task was a modification of the comparison task used by Thompson-Schill *et al* (1997). Subjects were told that they would see some cards and that they would have to choose words that matched each other on a particular dimension. They were shown a practice item (see figure 6.1 for examples), and told:

Figure 6.1: Sample Stimulus Cards from the Encoding Specificity Task



"On each card, the dimension I want you to think of is written first. Here it is "shape", so you need to be thinking about shape. Then there is a word, here it is "rhubarb", and I want you to choose which of the words in the box matches that word with respect to shape. Which word matches "rhubarb" when you're thinking about its shape?" The correct answer in this case was "leek", and the reasons were explained to the subject. When the subject understood the procedure, they were told:

"On some cards there is a specific thing to think about, like shape, but on others it just says "Most Similar". Then I want you to choose the word that is generally similar. Here is an example. Which word is most similar to "wolf"? The correct answer in this case was "squirrel" and again the examiner made sure that the subject understood the reasoning behind this decision.

Each subject completed four practice cards with the examiner. They were then told that they would move onto the test cards, and warned that they should pay close attention as afterwards they would be asked to remember which words they had chosen. Each subject saw 30 test cards. 15 of these required judgements to be made on one of five specific dimensions, (Specific Dimension Condition), and 15 of these required judgements to be made on global similarity (Similar Condition). These conditions differed in terms of the amount of selection amongst relevant and irrelevant semantic information pertaining to each item that was required in order to make a response.

In the Specific Dimension condition, subjects were required to make judgements according to one of 5 dimensions of the target word: "It's colour", "Its shape", "Its function / What it is for", "Its size", and "Natural or man-made?". In each case the dimension was printed first, followed by the target word, and then two probe words for subjects to choose between. The target and two probe words in each case were drawn from a category of the Battig & Montague (1969) norms, so that they were all members of the same semantic category. However only one of the probe words matched the target word according to the specific dimension specified. Therefore much of the semantic information retrieved in response to the words would not enable subjects to choose the correct probe word – they would have to select from the available semantic information and concentrate only on the specified dimension.

The other 15 cards required judgements to be made on global similarity. On these cards "Most Similar" appeared first to guide subjects' judgement process, followed by the target word, and finally four probe words. Following Thompson-Schill *et al* (1997), four probe words rather than two were used in this condition in order to match response times

and difficulty to the Specific Dimension condition. In this condition, the target word and correct probe word were drawn from the same category of the Battig & Montague (1969) norms, and the other three distractor probes were drawn from different categories. In this condition therefore all semantic information retrieved by the subjects would be relevant in choosing the correct probe word.

Fifteen categories from the Battig & Montague (1969) norms were used for the 30 problems, so that the same category of words appeared in one "Similar Condition" judgement, and one "Specific Dimension" judgement. This increased confusion between the items in the subsequent memory test, and was designed to elicit intrusions. Of the 30 problems, 15 used high frequency words (frequency of 50 or above in the Battig & Montague norms) and 15 used low frequency words (frequency of 10 or below in the Battig & Montague norms). All stimuli can be seen in Appendix 7.

Participants' responses to each card were recorded by the examiner. After administration of all 30 cards, the examiner read each target word out loud to the participant, who was asked to recall which word they had chosen to match it.

This test examined:

i) Retrieval and use of semantic information in order to make decisions at encoding. If the left IFG is involved with retrieval and use of semantic knowledge in general then one would expect those patients with damage to this region to have difficulty making the correct matching decision at encoding in both the Specific Dimension and the Similar condition. If however the left IFG is specialised for selecting among competing semantic information, we should expect a deficit only in the Specific Dimension condition.

ii) Subsequent recall of probe words, and the effects of the encoding condition (Similar or Specific Dimension) on recall rates. Firstly in a general sense we might expect higher rates of correct recall in the Specific Dimension condition than the Similar condition due to a levels of processing effect (Craik &

Lockhart, 1972; Craik, 2002). The Specific Dimension condition requires more elaborated encoding that should lead to higher recall. However, if poor recall performance amongst those with left IFG damage is due to an encoding deficit resulting from an inability to select the appropriate semantic information from competing alternatives, this would prevent elaborated encoding, and we would expect a reduced levels-of-processing effect in this group with more similar recall rates in the two conditions.

iii) Whether recall deficits are due to difficulties at encoding or retrieval. If recall impairment is due to an encoding deficit, then any difference in recall performance between groups should be dependent on their performance at encoding. Specifically if the left IFG subserves use of semantic knowledge in general, we should expect a recall deficit in both the Specific Dimension and the Similar conditions that disappears when those items that were incorrectly encoded are excluded from analysis. If Thompson-Schill *et al*'s theory is correct then we should expect this encoding dependent recall deficit only on the Specific Dimension condition. Of course if recall performance is more dependent on *retrieval* strategy, recall performance should not be linked to performance at encoding.

iv) The rates of intrusions at recall. Greater rates of intrusions induced by confusion between exemplars drawn from the same semantic category may be hypothesized to reflect an inability to correctly "bind" features of an episode together (Schacter *et al* 1998), possibly due to a breakdown in the formation of contextual bonds between memory fragments (Damasio *et al*, 1985b). Levels of processing theory would predict that levels of intrusions should be higher in the "Similar Condition" than in the "Specific Dimension" condition due to less elaborated encoding processes.

6.3 RESULTS:

Scoring:

The number of correct choices made at the encoding stage was recorded for all participants in each condition. Recall was scored in two ways. First the rates of recall over all words, regardless of whether the correct choice had been made at encoding, was recorded for each condition (raw recall). If the participant recalled the same word as they initially chose at the encoding stage, this was coded as correct. Secondly, to partial out the effects of choice at encoding, items for which the incorrect choice was made at encoding were excluded, so subsequent recall performance was recorded as a percentage of those items chosen correctly at encoding. Intrusions were categorised into three types: a) where the incorrect alternative from the correct item was recalled (e.g. recalling "pumpkin" for the target word "rhubarb" in the example above); b) recalling a presented word but from a different pair (e.g. recalling "squirrel" for the target word "rhubarb"). This category also included words recalled from the correct semantic category but from the wrong condition; c) providing a new, non-presented word. Intrusion rates were recorded as a percentage of those items for which the correct choice was made at encoding, as it was only for these items that correct and incorrect items could be clearly defined.

Correction for Guessing:

In order to control for guessed responses, the data were corrected in the following way. Measured encoding rates were assumed to consist of three components: 1) actual correct encoding (ACE), 2) measured correct encoding that was actually guessed (MCEG), and 3) measured incorrect encoding that was actually guessed (MIEG). If MCE = measured correct encoding, then these two formulae follow:

MCE = ACE + MCEG

And:

MIEG = 15-MCE

Given the number of choices across which guessing is taking place, the ratio between MCEG and MIEG is assumed to be 1:1 for the specific condition (in which there were two response options), and 1:3 for the Similar condition (in which there were 4 response options). This means that the actual correct encoding rates corrected for guessing are[12]:

For the Specific Dimension condition: $ACE = MCE - (15\text{-}MCE)$

For the Similar condition: $ACE = MCE - 1/3\ (15\text{-}MCE)$

Similarly, measured recall rates were assumed to consist of three components: 1) correct recall given actual correct encoding (CRE), 2) correct recall for guessed encoding (CRG), and 3) incorrect recall for guessed encoding (IRG).

$$\text{Actual Correct Recall (ACR)} = \frac{\text{Raw Recall} - \text{Recall given Guessed Encoding}}{\text{Actual Correct Encoding}}$$

$$= \frac{\text{Raw Recall} - (\text{CRG-IRG})}{\text{Actual Correct Encoding}}$$

If we assume CRG = IRG for the reasons given earlier, then actual correct recall (ACR) is given by the following formulae[13]:

For the Specific Dimension condition:

$$\text{Actual Corrected Recall} = \frac{2\ \text{Correct Recall Given Correct Encoding} - \text{Raw Recall}}{(2\ \text{MCE}) - 15}$$

For the Similar condition:

$$\text{Actual Corrected Recall} = \frac{4/3\ \text{Correct Recall Given Correct Encoding} - 1/3\ \text{Raw Recall}}{(4/3\ \text{MCE}) - 5}$$

[12] If the resulting figure was negative, it was converted to an actual corrected encoding score of 0.
[13] If the resulting figure was negative, it was converted to an actual correct recall rate of 0, and if the resulting figure was > 1 it was converted to an actual correct recall rate of 1.

The results from the encoding specificity task can be seen in table 6.1.

Table 6.1:
Encoding and Recall Performance on the Encoding Specificity Task

	Frontal	**Posterior**	**Control**
N	40	13	50
SPECIFIC DIMENSION			
Measured Correct Encoding (Max 15)	12.75 (2.24)	12.08 (2.60)	14.20 (1.05)
Actual Correct Encoding, ACE	10.53 (4.41)	9.23 (5.04)	13.40 (2.10)
Raw Recall (Max 15)	8.36 (4.00)	5.85 (4.00)	10.88 (2.95)
The following rates as a percentage of those items encoded correctly:			
Correct Recall Given Correct Encoding (%)	55.18 (28.09)	39.61 (27.26)	72.61 (19.32)
Actual Corrected Recall, ACR (%)	57.00 (34.00)	50.00 (31.00)	73.00 (20.00)
Intrusions (%)	16.93 (18.19)	25.70 (17.96)	12.28 (9.16)
Incorrect alternative	1.27 (2.81)	1.03 (2.50)	0.62 (2.13)
Previous item	8.67 (8.57)	15.31 (12.87)	9.68 (7.20)
New word	6.98 (13.03)	9.36 (13.14)	1.98 (4.23)
Don't Know (%)	27.89 (22.32)	34.68 (24.54)	15.11 (15.58)
SIMILAR CONDITION			
Measured Correct Encoding (Max 15)	13.05 (3.35)	13.15 (2.94)	14.52 (0.76)
Actual Correct Encoding, ACE	12.49 (4.16)	12.54 (3.92)	14.36 (1.02)
Raw recall (Max 15)	4.53 (2.84)	3.69 (2.81)	6.48 (2.83)
The following rates as a percentage of those items encoded correctly:			
Correct Recall Given Correct Encoding (%)	28.77 (20.91)	25.97 (19.00)	42.29 (19.47)
Actual Corrected Recall, ACR (%)	29.00 (22.00)	27.00 (20.00)	42.00 (20.00)
Intrusions (%)	29.88 (18.80)	28.95 (19.79)	19.67 (12.35)
Incorrect alternative	0.19 (1.22)	0.51 (1.85)	0.0 (0.00)
Previous item	19.78 (14.54)	17.99 (13.31)	16.35 (11.31)
New word	9.91 (15.33)	10.44 (12.80)	3.32 (5.70)
Don't Know (%)	41.35 (20.77)	45.08 (16.06)	38.04 (18.80)

Choice at Encoding:

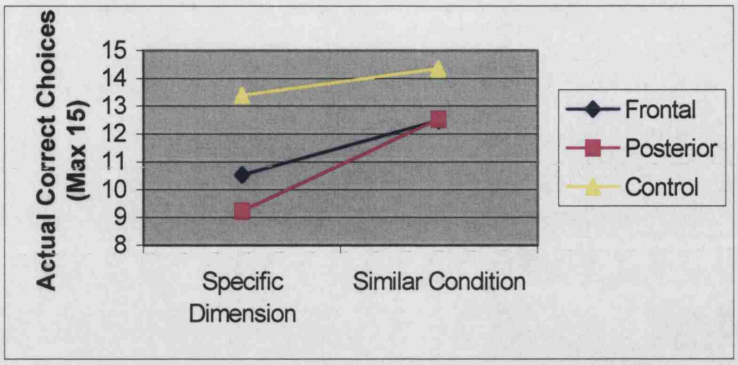


Figure 6.2: Actual Correct Choice at Encoding (Corrected for Guessing)

The number of actual correct choices made at the encoding stage (corrected for guessing) was analysed using a mixed model ANOVA with Group as the between-subjects variable and Condition (Specific Dimension or Similar) as the within-subjects variable. This revealed a significant effect of Condition ($F_{(1, 98)} = 9.26$, $p = 0.003$), with more correct choices being made in the Similar than in the Specific Dimension condition. There was also a significant effect of Group ($F_{(2, 98)} = 9.06$, $p = 0.000$), with a significant covariate of years of education ($F_{(1, 98)} = 5.87$, $p = 0.02$). Despite transformation Levene's test for equality of error variances was significant for the Similar condition ($F_{(2,100)} = 7.02$, $p = 0.001$). However subsequent Kruskal-Wallis tests for both conditions combined confirmed the significance of the group difference ($\chi^2 = 13.78$, $df = 2$, $p = 0.001$). Pairwise Mann-Whitney U comparisons confirmed that both the Frontal group ($U = 611.00$, $p = 0.001$) and the Posterior group ($U = 166.00$, $p = 0.006$) made significantly fewer correct choices than the Control group. There was no significant Condition by Group interaction ($F_{(2, 98)} = 1.95$ $p = 0.15$).

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group revealed the following results (see table 6.2 and figure 6.3).

Table 6.2:
Actual Correct Choices at Encoding: Grouping / Analysis Level 2.

	Orbital	Medial	L Lateral	R Lateral	Control
N	12	8	9	7	50
Actual Correct Choices Specific Condition	12.00 (3.57)	10.75 (4.20)	9.78 (5.78)	10.43 (4.72)	13.40 (2.10)
Actual Correct Choices Similar Condition	13.22 (2.97)	10.96 (6.34)	12.04 (4.46)	14.43 (1.51)	14.36 (1.02)

A mixed model ANOVA with Frontal Subgroup as the between-subjects variable and Condition (Specific Dimension or Similar) as the within-subjects variable revealed a significant effect of Condition ($F_{(1, 79)} = 10.49$, $p = 0.002$), with more correct choices being produced in the Similar condition than the Specific Dimension condition. There was also a significant effect of Frontal Subgroup ($F_{(4, 79)} = 3.61$, $p = 0.009$), with a significant covariate of years of education ($F_{(1, 79)} = 5.33$, $p = 0.02$). However despite transformation of the data Levene's test for equality of error variances was significant for the Similar condition ($F_{(4, 81)} = 4.92$, $p = 0.001$), and a subsequent Kruskal-Wallis test for both conditions combined did not confirm the significance of the group difference ($\chi^2 = 7.70$, $df = 4$, $p = 0.10$). There was no significant Condition by Frontal Subgroup interaction ($F_{(4, 79)} = 1.13$ $p = 0.35$).

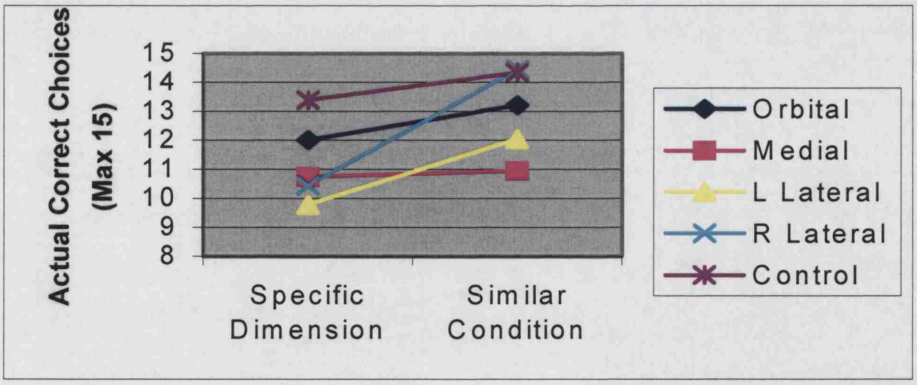


Figure 6.3: Actual Correct Choices at Encoding: Grouping / Analysis Level 2

Because of the rationale of the experiment, and the hypothesised significance of the left frontal lobe, planned comparisons were carried out comparing the Left Lateral group to

the Control group, even in the absence of a significant Frontal Subgroup difference. However independent samples t-tests revealed no significant difference between the Control and Left Lateral group on actual correct encoding rates in either the Specific Dimension condition ($t_{(8.38)} = -1.86$, $p = 0.10$) or the Similar condition ($t_{(8.15)} = -1.55$, $p = 0.16$).

Analysis at the third level revealed no significant results for the Specific Dimension condition (see Appendix 8 refs 3.1, 4.1, 5.1, 6.1), but the following results for correct choices in the Similar condition.

Table 6.3:
Actual Correct Choices at Encoding in the Similar Condition: Grouping / Analysis Level 3.

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 18 11.66 (4.12)	N = 12 11.64 (5.23)	N = 14 11.76 (4.14)	N = 11 14.39 (1.38)
Area Not Damaged Mean Score (SD)	N = 20 12.98 (4.32)	N = 26 12.69 (3.74)	N = 24 12.71 (4.32)	N = 27 11.53 (4.71)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with Right Lateral frontal damage performed significantly better at correctly choosing similar items at encoding than patients who did not have damage to this region ($t_{(34.17)} = -2.87$, $p = 0.007$). In fact the performance of this group was almost identical to the Controls.

Performance at Recall:

1) Raw Recall

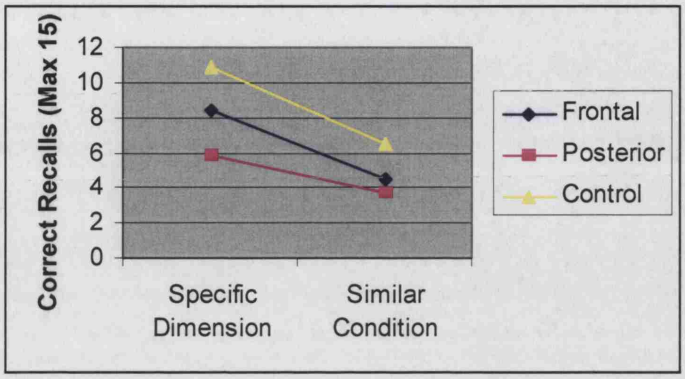


Figure 6.4: Correct Raw Recall Rates

Raw correct recall performance (see figure 6.4) was analysed using a mixed model ANOVA with Group as the between-subjects variable and Condition (Specific Dimension or Similar) as the within-subjects variable[14]. This revealed a significant effect of Condition ($F_{(1, 100)} = 123.72$, $p = 0.000$), with all groups recalling more words from the Specific Dimension condition than the Similar condition. There was also a significant effect of Group ($F_{(2, 98)} = 12.91$, $p = 0.000$) with a significant covariate of age ($F_{(1, 98)} = 9.38$, $p = 0.003$). Pairwise comparisons revealed that both the Frontal ($p = 0.000$) and the Posterior ($p = 0.000$) groups had significantly lower rates of correct recall than the Control group.

There was also a significant Condition x Group interaction ($F_{(2, 98)} = 6.02$ $p = 0.003$). Examination of figure 6.4 suggests that the Frontal and Control groups have a very similar drop off in recall performance in the Similar condition compared to the Specific Dimension condition, but that this drop off is less marked for the Posterior group. However simple main effects analysis found no differences in performance. Paired t-tests comparing performance in the Similar and Specific Dimension condition showed a

[14] Incorporating Years of Education as a covariate in these analyses had a complex effect on the within-subjects factor (Condition), due to a significant Condition x Years of Education interaction. As covariates should not impact on the within-subjects factor, results are only reported with covariates for the between-subjects factor (Group), and are reported without covariates for the within-subjects factor (Condition). The error terms in these analyses therefore differ.

significant difference for the Control ($t_{(49)} = 11.74$, $p = 0.000$), Frontal ($t_{(39)} = 8.89$, $p = 0.000$) and Posterior ($t_{(12)} = 3.55$, $p = 0.004$) groups. Similarly one–way ANOVAs revealed a significant effect of Group in both the Specific Dimension ($F_{(2, 98)} = 13.10$, $p = 0.000$) and Similar ($F_{(2, 98)} = 8.93$, $p = 0.000$) conditions. The Frontal and Posterior groups both differed from Controls in each ($p < 0.005$), but did not differ from each other. The reasons for the interaction therefore remain unclear.

Further exploration of whether this recall deficit might be specific to a particular subset of the Frontal group revealed the following results (Table 6.4 and Figure 6.5).

Table 6.4:
Raw recall rates: Grouping / Analysis Level 2

	Orbital Mean (SD)	**Medial Mean (SD)**	**L Lateral Mean (SD)**	**R Lateral Mean (SD)**	**Control Mean (SD)**
N	12	8	9	7	50
Correct Recall /15 Specific Dimension Condition	9.08 (5.12)	6.88 (4.42)	8.11 (2.89)	9.14 (2.54)	10.88 (2.95)
Correct Recall /15 Similar Condition	5.42 (3.63)	4.00 (2.39)	3.89 (3.10)	4.43 (0.98)	6.48 (2.83)

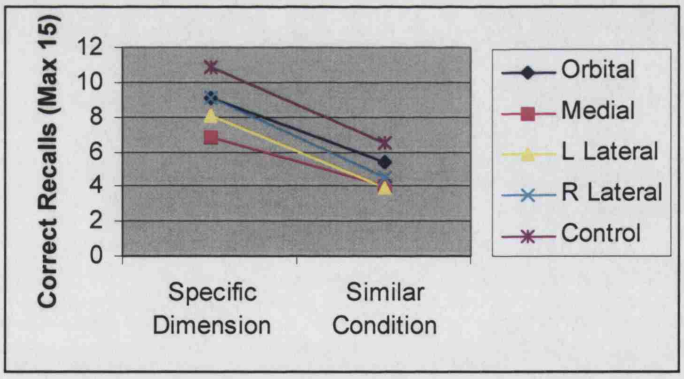


Figure 6.5: Correct Raw Recall Rates: Grouping / Analysis Level 2

A mixed model ANOVA with Frontal Subgroup as the between-subjects variable and Condition (Specific Dimension or Similar) as the within-subjects variable again revealed a significant effect of Condition ($F_{(1, 81)} = 106.57$, $p = 0.00$) and a significant effect of Frontal Subgroup ($F_{(4, 79)} = 4.02$, $p = 0.005$), with a significant covariate of age ($F_{(1, 79)} = 9.58$, $p = 0.003$). Levene's test was significant indicating that error variances for the

Frontal Subgroups were unequal in the Specific Dimension condition ($F_{(4, 81)} = 4.83$, $p = 0.02$). However a subsequent Kruskal-Wallis test using combined recall rates from the Specific Dimension and Similar conditions confirmed that there was a significant effect of Frontal Subgroup ($\chi^2 = 12.28$, $df = 4$, $p = 0.02$) Pairwise Mann-Whitney U comparisons confirmed that the Medial ($U = 87.50$, $p = 0.009$), Left Lateral ($U = 109.00$, $p = 0.014$) and Right Lateral ($U = 91.50$, $p = 0.04$) groups recalled significantly fewer words than the Control group. There was no significant Condition by Frontal Subgroup interaction ($F_{(4, 79)} = 1.25$ $p = 0.30$).

Again due to the specific hypothesis relating to the Left Lateral group, planned comparisons were carried out comparing the performance of this group to Controls in raw recall in both conditions separately. This revealed that the Left Lateral group had significantly lower recall rates in both the Specific Dimension ($t_{(57)} = -2.60$, $p = 0.01$) and the Similar conditions ($t_{(57)} = -2.49$, $p = 0.02$).

Analysis at the third level revealed no significant results (see Appendix 8 refs 3.2, 3.3, 4.2, 4.3, 5.2, 5.3, 6.2, 6.3).

2) Recall Performance for Correctly Encoded Items

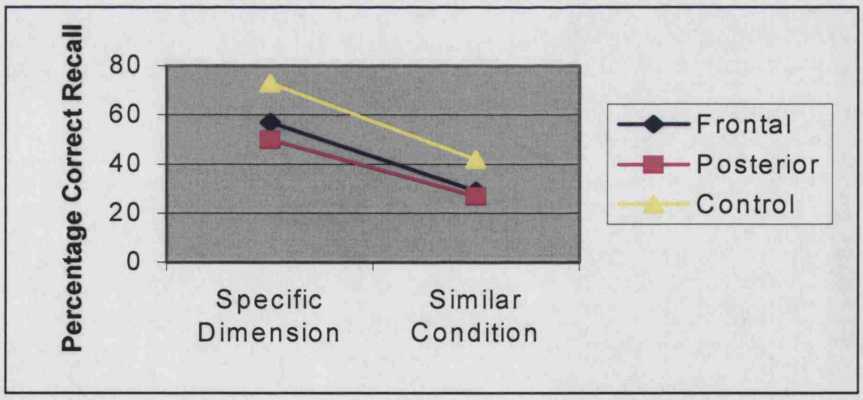


Figure 6.6: Correct Recall For Items Correctly Encoded

In order to partial out the effects of problems at encoding on recall rates, analysis of actual correct recall only for those items which had been correctly encoded was conducted (see figure 6.6). If the recall deficit in the Frontal group is due to failures at the encoding stage, then this recall deficit should disappear when recall performance is examined only for those items that were encoded correctly. A mixed model ANOVA with Group as the between-subjects variable and Condition (Specific Dimension or Similar) as the within-subjects variable revealed a significant effect of Condition ($F_{(1, 100)} = 82.92$, $p = 0.000$), with all groups recalling more words in the Specific Dimension condition than the Similar condition. There was also an effect of Group ($F_{(2, 98)} = 4.84$, $p = 0.01$). Levene's test for equality of error variances was significant for recall in the Specific Dimension condition ($F_{(2, 100)} = 4.71$, $p = 0.01$). However a subsequent Kruskal Wallis test using combined actual corrected recall rates from the Specific Dimension and Similar conditions confirmed the significance of the Group difference ($\chi^2 = 10.73$, df = 2, $p = 0.005$). Pairwise Mann Whitney U comparisons revealed that both the Frontal ($p = 0.007$) and the Posterior ($p = 0.009$) groups had significantly lower rates of correct recall than the Control group. There was no significant Condition x Group interaction ($F_{(2, 98)} = 0.47$ $p = 0.62$).

Analysis at level 2 revealed no effect of Frontal Subgroup (see Appendix 8 ref 2.1). However planned comparisons comparing the Left Frontal group against the Control group revealed the following results.

Table 6.5:
Corrected Recall rates: Left Lateral Group vs Controls

	Left Lateral N = 9	Control N = 50
Actual Corrected Recall Rates – Specific Dimension Condition	61.46 % (32.28)	72.82% (19.58)
Actual Corrected Recall Rates – Similar Condition	25.46% (20.47)	41.85% (19.73)

In the Specific Dimension condition there was no difference between the rates of corrected recall ($t_{(9.09)} = -1.02$, $p = 0.33$). However there was a significant difference

between the corrected recall rates in the Similar condition ($t_{(57)} = -2.28$, $p = 0.03$), with the Left Lateral group recalling significantly fewer words than the Control group.

Analysis at Level 3 revealed no further results (see Appendix 8, refs 3.4, 3.5, 4.4, 4.5, 5.4, 5.5, 6.4, 6.5)

Specific Anatomical Analysis of the Left Inferior Frontal Gyrus Group:

Given the specific hypothesis that patients with damage to the left inferior frontal gyrus should be selectively impaired on aspects of this task, a new patient grouping was created in which those frontal patients with left IFG damage (N = 7) were compared to those without left IFG damage (N = 33). This group included 5 of those classified as L Lateral in the level 2 grouping (1 was previously unclassified, and 1 had been in the Medial group). Encoding and recall performance measures split by this new grouping can be seen in Table 6.6.

Table 6.6:
Encoding and Recall Performance for Patients With and Without Left IFG Damage

	Left IFG Damage N = 7 Mean (SD)	No Left IFG Damage N = 33 Mean (SD)
Actual Correct Encoding /15 (Specific Dimension Condition)	9.71 (5.44)	10.70 (4.25)
Actual Correct Encoding /15 (Similar Condition)	11.76 (4.06)	12.65 (4.22)
Raw Recall / 15 (Specific Dimension Condition)	7.43 (4.31)	8.03 (4.20)
Raw Recall / 15 (Similar Condition)	3.43 (3.05)	4.45 (2.86)
Actual Corrected Recall (Specific Dimension Condition)	48.00 (37.00)	59.00 (33.00)
Actual Corrected Recall (Similar Condition)	24.00 (20.00)	30.00 (23.00)

The analyses previously conducted were repeated using this grouping to examine whether possible left IFG effects had being masked by the heterogeneous nature of the damage in our L Lateral group. However there were no effects of Group or Group x Condition interactions in any analysis of encoding or recall (**Actual Correct Encoding**: IFG Group $F_{(1, 36)} = 0.40$, $p = 0.53$; Condition $F_{(1, 36)} = 6.11$, $p = 0.02$; IFG Group x Condition $F_{(1, 36)}$

= 0.18, p = 0.67; **Raw Recall**: IFG Group $F_{(1, 37)} = 0.75$, p = 0.39; Condition $F_{(1, 37)} = 13.62$, p = 0.001; IFG Group x Condition $F_{(1, 37)} = 0.02$, p = 0.98; **Actual Corrected Recall:** IFG Group $F_{(1, 36)} = 1.69$, p = 0.20; Condition $F_{(1, 36)} = 1.45$, p = 0.24; IFG Group x Condition $F_{(1, 36)} = 0.30$, p = 0.59).

Intrusions:

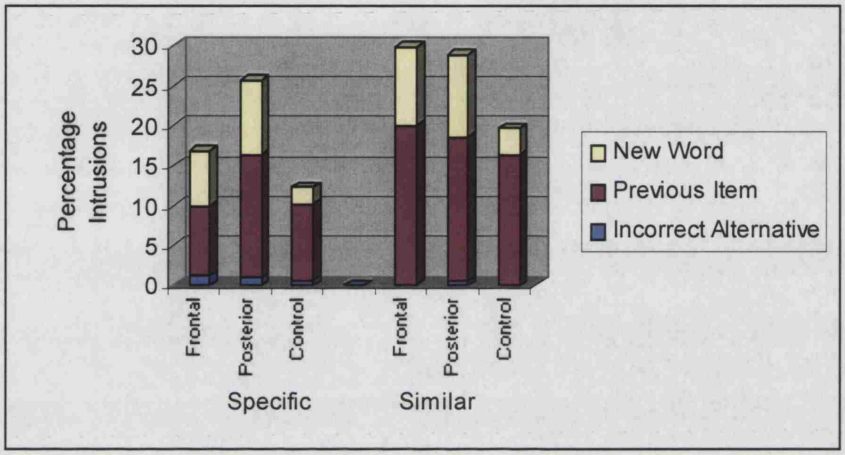


Figure 6.7: Intrusion Rates

Analysis of overall intrusion rates using a mixed model ANOVA with Condition as the within-subjects factor and Group as the between subjects factor revealed no significant effects (Condition: $F_{(1, 99)} = 0.62$, p = 0.43; Group: $F_{(2, 99)} = 1.74$, p = 0.18; Condition x Group interaction: $F_{(2, 99)} = 0.85$ p = 0.43). This analysis was then conducted for each type of intrusion separately. For recall of the incorrect alternative from the original encoding choice there were no significant effects (Condition: $F_{(1, 99)} = 3.86$, p = 0.052; Group: $F_{(2, 99)} = 1.58$, p = 0.21; Condition x Group interaction: $F_{(2, 99)} = 0.39$ p = 0.68). For recall of a correct word but from an incorrect, previous exemplar there were also no significant effects (Condition: $F_{(1, 99)} = 1.16$, p = 0.29; Group: $F_{(2, 99)} = 0.10$, p = 0.91; Condition x Group interaction: $F_{(2, 99)} = 1.02$ p = 0.39). However for recall of a completely new word, although there was no effect of Condition ($F_{(1, 99)} = 2.57$, p = 0.11) nor a Condition x Group interaction ($F_{(2, 99)} = 0.02$ p = 0.98), there was a significant effect of Group ($F_{(2, 99)} = 6.10$ p = 0.003). Levene's test for equality of error variances was significant for the Specific Dimension condition ($F_{(2,100)} = 10.61$, p = 0.000) and for

the Similar condition ($F_{(2,100)} = 6.54$, $p = 0.002$). However a subsequent Kruskal-Wallis test using new intrusion rates combined across both conditions confirmed the group difference ($\chi^2 = 8.76$, $df = 2$, $p = 0.02$). Pairwise Mann-Whitney U comparisons revealed that both the Frontal ($U = 706.50$, $p = 0.013$) and the Posterior ($U = 196.00$, $p = 0.02$) groups produced significantly more new words than the Control group.

More detailed anatomical analysis at the second level revealed the following results.

Table 6.7:
Mean Intrusions: Grouping / Analysis Level 2.
(All rates as a percentage of those items encoded correctly)

	Orbital Mean (SD)	**Medial Mean (SD)**	**L Lateral Mean (SD)**	**R Lateral Mean (SD)**	**Control Mean (SD)**
N	12	8	9	7	50
SPECIFIC DIMENSION					
Intrusions (%)	16.92 (16.17)	16.11 (26.01)	14.60 (8.60)	12.65 (10.22)	12.28 (9.16)
Incorrect alternative	1.85 (3.36)	1.79 (3.33)	0.00 (0.00)	0.95 (2.52)	0.62 (2.13)
Previous item	8.39 (8.86)	6.79 (11.82)	8.86 (6.52)	9.45 (9.30)	9.68 (7.20)
New word	6.68 (8.39)	7.52 (15.35)	5.74 (10.31)	2.25 (3.91)	1.98 (4.23)
SIMILAR					
Intrusions (%)	30.47 (17.40)	22.60 (24.77)	33.10 (14.59)	26.91 (13.93)	19.67 (12.35)
Incorrect alternative	0.64 (2.22)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)
Previous item	25.07 (16.97)	9.25 (8.13)	27.05 (11.79)	17.14 (10.79)	16.35 (11.31)
New word	4.76 (9.30)	13.34 (19.23)	6.05 (8.65)	9.05 (7.38)	3.32 (5.70)

Analysis of overall intrusions rates using a mixed model ANOVA with Condition as the within-subjects factor and Frontal Subgroup as the between subjects factor revealed no significant effects (Condition: $F_{(1, 80)} = 2.72$, $p = 0.10$; Frontal Subgroup: $F_{(4, 80)} = 1.37$, $p = 0.25$; Condition x Frontal Subgroup interaction: $F_{(4, 80)} = 0.55$ $p = 0.70$). This analysis was then conducted for each type of intrusion separately.

For recall of the incorrect alternative from the original encoding choice there was no significant effect of Frontal Subgroup ($F_{(4, 80)} = 1.77$, $p = 0.14$) but there was a significant effect of Condition ($F_{(1, 80)} = 4.42$, $p = 0.03$), with more incorrect alternatives being recalled in the Specific Dimension condition than in the Similar condition. There was no Condition x Frontal Subgroup interaction: $F_{(2, 99)} = 0.39$ $p = 0.68$).

For recall of a correct word but from an incorrect, previous exemplar there were no significant effects (Condition: $F_{(1, 80)} = 3.40$, $p = 0.07$; Frontal Subgroup: $F_{(4, 80)} = 1.47$, $p = 0.22$; Condition x Frontal Subgroup interaction: $F_{(4, 80)} = 1.00$ $p = 0.41$).

However for recall of a completely new word, there was no significant effect of Frontal Subgroup ($F_{(4, 80)} = 1.70$, $p = 0.16$) but there was a significant effect of Condition ($F_{(1, 80)} = 4.12$, $p = 0.046$, with more new words being recalled in the Similar condition than in the Specific Dimension condition. There was no Condition x Frontal Subgroup interaction ($F_{(4, 80)} = 1.86$ $p = 0.13$).

Analysis at the third level was conducted for rates of new intrusions only, as this was the only variable to yield a significant Frontal effect at level 1. For the Similar condition, no effects were found (see Appendix 8, refs 3.6, 4.6, 5.6, 6.6). However for the specific condition the following effects were found.

Table 6.8:
Percentage New Intrusions: Specific Dimension Condition: Grouping / Analysis Level 3.

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 18 6.35 (7.20)	N = 12 11.33 (21.58)	N = 14 8.80 (17.43)	N = 11 1.43 (3.23)
Area Not Damaged Mean Score (SD)	N = 20 8.25 (17.17)	N = 26 5.51 (6.80)	N = 24 6.50 (10.47)	N = 27 9.76 (15.03)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the right lateral region produced significantly fewer new intrusions in their recall in the Specific Dimension condition than those without damage to this area ($t_{(31.19)} = 2.73$, $p = 0.01$).

6.4 DISCUSSION:

Encoding:

Performance at encoding revealed a significant effect of condition, with more correct choices being made in the Similar condition than in the Specific Dimension condition in

all groups. There was also a significant effect of patient group on correct choices at encoding, with the Frontal and Posterior groups making significantly more errors in their selection of the correct pairs than the Control group. However there was no Group x Condition interaction, and no more specific subgroup effects at the second level of analysis. At the third level of analysis those patients with right lateral damage made significantly more correct choices in the Similar condition than those without damage to this region.

The results of Thompson-Schill *et al* (1997) would have predicted a specific reduction in the number of correct choices made by patients with damage involving the left inferior frontal gyrus in the Specific Dimension condition, due to difficulty in selecting the relevant semantic information required to make the match amongst competing alternatives. We found a reduced correct encoding effect in the Frontal group as a whole in the Specific Dimension condition, but not a specific deficit in our Left Lateral patients, even when planned comparisons comparing the Left Lateral group against the Controls were carried out. Instead our Frontal group as a whole were poorer at making encoding decisions in both conditions, and all groups, including the Controls, found the Specific Dimension condition more difficult than the Similar condition. This result implies that our Frontal group as a whole experienced difficulty in retrieving or using semantic knowledge to make their encoding decisions, whether selection was involved or not, and whether they had left IFG damage or not. However it would be rash to treat this as definitive negative evidence for the link between encoding processes and the left VLPFC. The numbers of patients in our frontal subgroups are small, and this may have concealed trends that were actually present. Indeed there was a trend in the more detailed anatomical analysis suggesting that the L Lateral and R Lateral subgroups were far more impaired at the encoding stage in the Specific Dimension condition than the Similar condition. Certainly the Right Lateral group were preserved at making correct choices at encoding in the Similar condition as revealed by the level 3 analysis. The Medial group in contrast appeared to be impaired compared to controls in both conditions. However these apparent trends were not supported by non-parametric analysis.

Recall:

In terms of recall performance, we found a clear effect of encoding condition, with more words being recalled from the Specific Dimension condition than from the Similar condition. This result is to be expected as the Specific Dimension condition requires more elaborated encoding of material and according to levels of processing theory should therefore result in higher recall. However we did not find an interaction suggesting a reduction in this levels of processing effect amongst the Left Lateral group, which might have been expected if this group had more difficulty in conducting the elaborated encoding required for the Specific Dimension condition.

In terms of group effects, the data revealed that the Frontal and Posterior patients had significantly lower levels of recall than the Controls, on both raw and corrected recall rates. The second level of analysis revealed that the Medial, Left Lateral and Right Lateral subgroups all had reduced raw recall rates compared to the Controls, but this Frontal Subgroup effect was no longer present when only recall of those items successfully encoded was examined (corrected recall). No level 3 effects were found, but planned comparisons comparing the Left Lateral group to the Controls revealed that they had significantly reduced corrected recall in the Similar condition.

Thompson-Schill *et al*'s (1997) theory would predict that those patients with left IFG damage should show reduced recall rates in the specific condition when overall raw recall was examined, but that this impairment would be due to difficulties at the encoding stage. Therefore if recall rates are examined only for those items which were correctly encoded, this difference should disappear. More general left frontal–encoding theories would predict a recall deficit in both the Specific and Similar conditions in raw recall, which disappeared when recall was corrected for performance at encoding. In initial analysis by ANOVA, our data did not support Thompson-Schill *et al*'s theory, but provided some support for a general left frontal role (amongst other areas) in encoding processes. The Frontal group as a whole had impaired recall when both raw and corrected rates were examined. Their poor recall is not fully explained by performance at encoding, indicating that it is due to a combination of impaired encoding and retrieval strategies. However

when specific subgroups were examined we found that the Medial, Left Lateral and Right Lateral groups had significantly lower raw recall rates than the Controls, but that this deficit disappeared when recall rates were corrected for performance at encoding. This indicates that in all three of these groups, their reduced recall was to some extent due to faulty encoding processes, presumably related to an inability to retrieve and use semantic knowledge in their encoding decisions. We found no interactions which would have implied that this was due in particular to the Specific Dimension condition.

However planned comparisons comparing the Left Lateral group to the Control group revealed slightly different results. In raw recall the Left Lateral group had significantly lower recall rates than the Controls in both the Specific Dimension and the Similar condition. However when corrected recall was examined they differed from Controls only in the Similar condition, and recall rates in the Specific Dimension condition were comparable to Controls. This seems to provide some support for Thompson-Schill *et al*'s hypothesis, in that it appears that the Left Lateral group's recall impairment in the Specific Dimension condition was due to difficulties at encoding. However planned comparisons failed to reveal any Left Lateral encoding deficit in either condition which would be predicted by their theory. Whilst small group sizes undoubtedly will have affected the sensitivity of these measures to specific subgroup effects, it would be unwarranted on the basis of these data to conclude that the Left Lateral group have a specific inability to select between competing semantic features. Instead we can conclude only that our data indicate a recall deficit in the Left Lateral, Right Lateral and Medial groups which is at least in part due to difficulties at the encoding stage. More specific conclusions about lesion specificity, and about which specific encoding processes are impaired, would require further investigation with larger sample sizes.

It might be argued that the Left Lateral effects observed here provide support for a general left VLPFC role in the retrieval and use of semantic knowledge to make encoding decisions that results in a subsequent recall impairment (Demb *et al*, 1995; Gabrieli *et al*, 1996; Henson *et al*, 1999a; Tulving *et al*, 1994; Wagner *et al*, 1998c). However, although we found this effect in our Left Lateral subgroup, we did not find any effects when a

more specific analysis was conducted examining the performance of only those patients with left IFG damage. According to previous research (e.g. Baker *et al*, 2001; Fletcher *et al*, 1998, Henson *et al*, 1999a; Wagner *et al*, 1998c; Wig *et al*, 2004) this area specifically should underlie semantic encoding processes, so if anything we should have seen a stronger effect in this group. The lack of any effects here is indeed puzzling, but may be due to several reasons. Firstly we had only a small number of patients (N = 7) with left IFG damage, and of course each of these patients had damage to a variety of other areas in addition. Another possibility is that there may be a confound with size of lesion or site of major lesion. The level 2 groupings, where we did get the predicted effect, were based on the area of *majority* damage, so this was the group with the most extensive left lateral damage. There are possible connectivity implications here, and of course the not inconsiderable difficulty of precisely identifying regions of damage from MRI scans. Either way, activation in neuroimaging studies indicates involvement of a particular area in a particular process, but not the necessity of that area for the process. Our results raise the possibility that the left IFG may be involved but is not necessary for semantic encoding decisions.

It also seems puzzling that as well as our Left Lateral result we obtained an analogous pattern for the Medial and Right Lateral groups. All three subgroups showed a significant recall impairment compared to Controls in raw recall that disappeared when recall was corrected for performance at encoding. Medial regions have not previously been specifically associated with semantic encoding processes. However on closer examination of the literature it is evident that this pattern *has* been reported before despite the emphasis always being placed on the left IFG. Thompson-Schill *et al* (1997) actually found medial activation in *all* the same conditions as their left IFG activation, specifically in the anterior SMA and anterior cingulate. This had not been part of their primary hypothesis, but they ended by suggesting that whether the functions of these medial regions and the left IFG differed in any significant way would have to be further investigated. Similarly Henson *et al* (1999a) reported medial frontal and anterior cingulate cortex activation associated with "Remember" judgements in their paradigm, Wagner *et al* (1998c) reported medial superior frontal gyrus activation associated with

word processing at encoding, and Gabrieli *et al* (1996) reported greater left cingulate cortex activation in a semantic than a perceptual encoding task. Our results therefore provide some support for imaging findings in relation to both the left lateral and the medial region in a neuropsychological series. Whether these areas are involved in encoding in general, or specifically in semantic encoding, or whether they are differentially involved in the two is impossible to say as our paradigm did not include a non-semantic encoding condition, but given the convergence of findings clearly warrants further investigation. The Right Lateral deficit is more puzzling, as this region has previously been associated more with retrieval than with encoding processes (e.g. Cabeza *et al*, 1997a; Lepage *et al*, 2000; Tulving *et al*, 1994; Nyberg *et al*, 1996a; Wagner *et al* 1998a, see Chapter 1, section 1.4.1.2). It would appear from this data that poor recall in this group was at least partially accounted for by difficulties at encoding as well, and that this encoding deficit arose to a far greater extent in the Specific Dimension condition than the Similar condition.

Intrusions:

No Frontal effect was found in analysis of overall intrusion rates in this paradigm. However the Frontal group did produce significantly higher rates of completely new, non-presented words than the Control group. At the second level of analysis two condition effects were revealed, with higher rates of "incorrect alternative" intrusions in the Specific Dimension than the Similar condition, and conversely, higher rates of new word intrusions in the Similar than the Specific Dimension condition. This effect is explicable within the levels of processing framework. In the Specific Dimension condition subjects probably had to think about the semantic association of both possible words to the target in order to make the correct decision. Furthermore, both words in this condition were from the same semantic category as the target (whereas in the Similar condition only the correct answer was from the same semantic category as the target word). Therefore a stronger memory trace was made even for the incorrect associate in this condition than for the incorrect associates in the Similar condition. Possibly as a result of this, more new words were produced as intrusions in the Similar condition as

subjects were less likely to recall either the target or the incorrect associate, and produce a guess.

It might have been expected on the basis of results in the last two chapters that we would find higher rates of intrusions (perhaps specifically new word intrusions) in the Orbital and Medial subgroups (these two groups were associated with the presence of confabulations in the confabulation battery and with intrusions in the OM tasks). However no subgroup effects were found. This is likely to be at least in part a consequence of the large variances associated with this data. Unfortunately with some standard deviations being larger than the group mean in this task, analysis of intrusions was bound to be fairly insensitive. However at the third level of analysis, those patients with right lateral damage were found to produce fewer new word intrusions in the Specific Dimension condition than those without damage to this area, so this at least confirms the sparing of this group.

CHAPTER SEVEN:
REALITY MONITORING TASK

7.1 INTRODUCTION

Patients with frontal damage have frequently been reported to show deficits in memory for the source of information. Thus whilst item memory may be relatively preserved, memory for contextual information about where and when the information was encountered is impaired (Janowsky *et al*, 1989b; Johnson *et al*, 1997; Schacter *et al*, 1984; Shimamura *et al*, 1990; Ward & Parkin, 2000). This may be particularly marked when subjects are not instructed to remember the source of their memories, so that when this incidentally encoded information is later required, frontally controlled strategic retrieval processes must be implemented to access it (Kopelman *et al*, 1997b; Shimamura, 2002; Thaiss & Petrides, 2003).

One specific example of source monitoring, which has been associated with frontal dysfunction and confabulation, is reality monitoring (Johnson *et al*, 1993; Johnson, 1997). This process involves attributing an internal or external source to ones' experiences or memories, for example deciding whether you actually carried out an action or only thought about it. For example Ward & Parkin (2000) reported that their MS patient MR (with left frontal damage) could not distinguish between actions he had actually carried out, and actions he had only imagined (e.g. opening a can, blowing in the air). Instead he showed a tendency to misattribute imagined experiences to real events. Similarly Johnson *et al* (1997) reported that confabulating ACoA patient WL had a bias to report that items previously presented as words which she had imagined as pictures, had actually been presented to her in picture form. However Dalla Barba *et al* (1997) reported that confabulating ACoA patient GA, although she was impaired at a reality monitoring task, had no tendency to misattribute imagined events to real occurrences. Instead she made an equal number of "real" or "imagined" responses.

Imaging studies of source memory have generally reported that retrieval of source as opposed to item recognition tends to activate the left prefrontal cortex (Dobbins *et al*,

2002; Cansino *et al*, 2002; Fan *et al*, 2003; Nolde *et al*, 1998a; Nyberg *et al*, 1996b; Ranganath *et al*, 2000; Rugg *et al*, 1999). Others have reported activation of left and right lateral regions associated with retrieval of source (Cabeza *et al*, 2003; Henson *et al*, 1999b; Slotnick *et al*, 2003). Up until now only two imaging studies have been conducted which relate specifically to reality monitoring. Lundstrom, Petersson, Andersson, Johansson, Fransson & Ingvar (2003) presented subjects with visually presented words followed either by a picture of the object, or a blank screen which prompted subjects to imagine a picture of the object. They then scanned subjects during an item recognition task where subjects identified words as old or new, and a source memory task where subjects identified for old words whether they had previously viewed or imagined a picture of the object. They reported that left lateral prefrontal activation (BA 10, 9, 44, 45, 46 and 47) was greater in source memory than item recognition trials, and that a subset of these regions (BA 45, 46 and 47) were more active during retrieval of imagined rather than viewed pictures.

In the second study Simons, Owen, Fletcher & Burgess (submitted) attempted to image the difference between recall of internal and external context information. They scanned subjects whilst carrying out either a task context (internal) retrieval task (identifying which orienting task they had carried in relation to words at study) or a position context (external) retrieval task when they had to decide if stimulus item had been presented on the right or left side of screen. They found that activation of the medial aspect of left anterior PFC and bilateral ventromedial PFC was greater for the task context (internal) than for the position context (external) retrieval task. They argued that whilst left lateral PFC seems to play a general role in the processing of contextual information, the medial anterior region was preferentially involved when the retrieval cue required recollection of contextual details that were internally generated, e.g. the thought process engaged during study task performance. They concluded:

> "this region may be responsible for the subjective metacognitive experience of recollecting phenomenological details from the past. Future studies are required to establish how well these results generalise to other instances of internally generated remembering, such as for example distinguishing between recollection of events that were experienced as opposed to those that were

> imagined....On the basis of the present results it would be predicted that medial anterior PFC activation would be more strongly associated with the recollection of such internally-generated contextual information than with retrieving externally-derived perceptual details."

In fact the Dobbins *et al* (2002) experiment mentioned above actually used an orienting task identification judgement as their source retrieval condition so this is similar to the internal context task of Simons *et al* (submitted). Interestingly, they also reported an area of medial activation, although this was in the left superior frontal gyrus. Whilst the imaging studies are by no means consistent, these recent investigations do raise the intriguing possibility that medial regions may be more involved in internal/external reality monitoring processes than more lateral regions, which may be recruited more in external source judgements.

7.2 METHOD

To examine the ability of patients with frontal lobe damage to distinguish between real and imagined events, a reality monitoring task based on that developed by Aleman, Bocker, Hijman, de Haan, & Kahn (2003) for use with schizophrenic patients was developed. Subjects were given the following instructions:

"This test is to do with your memory for words. Sometimes I will read you some words normally, and sometimes I will ask you to imagine hearing some words. For example, I might ask you to imagine a colour beginning with "B". When I do this, I do not want you to say the word you think of out loud, but I want you to imagine the word being spoken"

When the examiner was confident that the participant had understood the procedure, she told the participant that in the test she would alternate between reading a word normally and asking them to imagine a word, and that if when she asked them to imagine a word they could not think of one before she read the next one, they should not worry but ignore it and move on.

The list was constructed by taking the first three associates from 15 categories from the Battig & Montague (1969) norms. One of these words was selected to be read normally, one to be imagined by the subject, and one to be used as a distractor in the subsequent memory test. Thus for the category "Metals", "copper" was read normally, subjects were asked to imagine a metal beginning with "I" (iron), and "steel" appeared as a distractor.

The examiner read the list of 30 items, comprising 15 words read normally alternated with 15 words that the subject was asked to imagine, out loud to each participant, at a rate of one every 4 seconds. Immediately after the last item was presented, the subject was told that the examiner was now going to read a list of words. For each one, they were asked to say whether they heard the examiner read the word, whether they imagined the word, or whether the word was new. The 45-word list (comprising the 15 words read earlier, the 15 words the subject had been asked to imagine, and the 15 distractor words) was then read out loud in a random order to the participant, whose responses were recorded by the examiner. Subjects were not pre-warned of this source memory component, and any encoding of internal or external source was therefore incidental. All stimuli for the task can be seen in Appendix 9.

7.3 RESULTS

Heard Items:

The pattern of responses for items which had been read aloud is illustrated in figure 7.1.

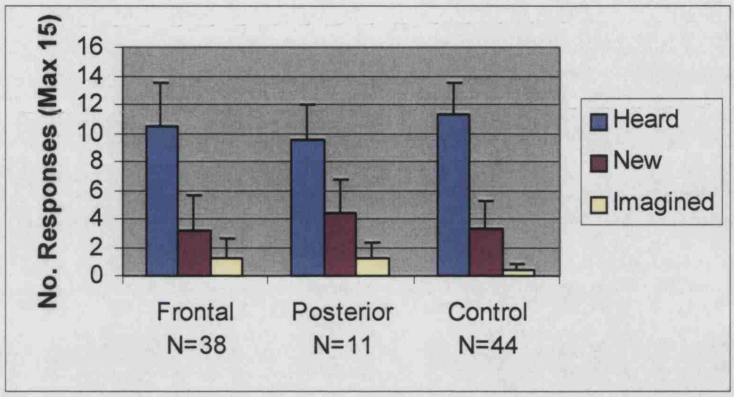


Figure 7.1: Pattern of Responses for Heard Items by Group

Three one-way ANOVAs on correct responses, items identified as imagined, and items identified as new revealed the following results[15]. There was no significant effect of Group for either correct responses ($F_{(2, 88)} = 2.72$, $p = 0.07$), or items incorrectly identified as "new" ($F_{(2, 88)} = 1.21$, $p = 0.31$). However there was a significant effect of Group on items incorrectly identified as "Imagined" ($F_{(2, 88)} = 4.89$, $p = 0.01$). Despite transformation Levene's test for equality of error variances was significant ($F_{(2, 90)} = 5.78$, $p = 0.04$). However a Kruskal Wallis test confirmed the Group effect ($\chi^2 = 8.08$, df $= 2$, $p = 0.02$) and pairwise Mann Whitney comparisons confirmed that the Frontal group produced significantly more incorrect "Imagined" responses than the Control group ($U = 603.00$, $p = 0.04$).

Further exploration of whether this deficit might be specific to a particular subset of the Frontal group yielded the following results.

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[15] The three response categories analysed here are not independent of each other. Analyses were conducted to avoid losing valuable information about group differences in patterns of responding, but caution is required in interpreting the results. To be conservative, the significance levels for Level 1 analyses have been subject to a Bonferroni correction of 2 (see Sankoh, Huque & Dubey, 1997). Analyses are therefore only considered significant if $p < 0.025$.

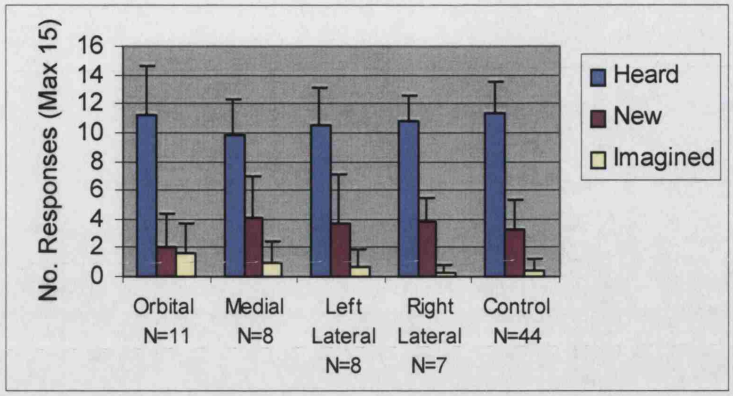

Figure 7.2: Pattern of Responses for Heard Items by Frontal Subgroup (Grouping / Analysis Level 2)

One-way ANOVAs revealed no significant effect of Frontal Subgroup for either correct responses ($F_{(4, 71)} = 0.98$, $p = 0.45$), or items incorrectly identified as "new" ($F_{(4, 71)} = 1.20$, $p = 0.32$). However there was a significant effect of Frontal Subgroup on items incorrectly identified as "Imagined" ($F_{(4, 71)} = 2.67$, $p = 0.04$). Despite transformation Levene's test for equality of error variances was significant ($F_{(4, 73)} = 3.99$, $p = 0.006$), and a subsequent Kruskal Wallis test failed to confirm the effect ($\chi^2 = 6.84$, $df = 4$, $p = 0.14$).

Following the significant Frontal effect at Level 1, analysis at level 3 was carried out for heard items incorrectly identified as imagined.

Table 7.1:
"Heard" Words Incorrectly Identified as "Imagined": Grouping / Analysis Level 3

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 2.12 (2.74)	N = 11 0.73 (0.90)	N = 13 1.62 (2.72)	N = 11 0.36 (0.67)
Area Not Damaged Mean Score (SD)	N = 19 0.58 (0.84)	N = 25 1.56 (2.42)	N = 23 1.13 (1.69)	N = 25 1.72 (2.37)

Independent samples t-tests were carried out for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the inferior medial region misidentified significantly more "Heard" words as "Imagined" than those without damage to this region ($t_{(18.68)} = -2.23$, p

= 0.04). Conversely, those with damage to the right lateral region made significantly fewer of these errors than those without damage to this area ($t_{(31.10)} = 2.63$, $p = 0.01$).

Imagined Items:

The pattern of responses for items which the subjects had previously been prompted to imagine is illustrated in figure 7.3.

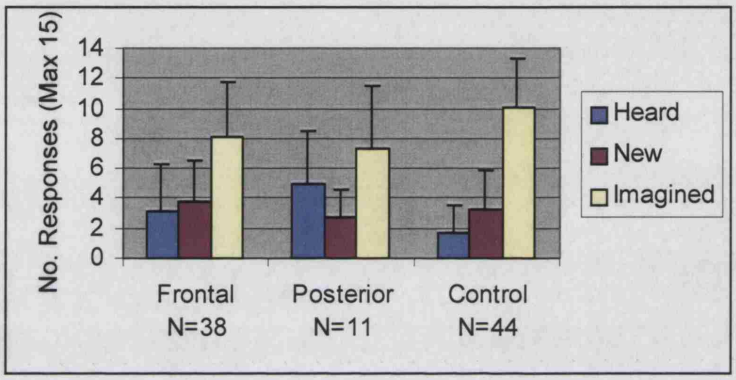

Figure 7.3: Pattern of Responses for Imagined Items by Group

One-way ANOVAs revealed a significant effect of Group on correct responses ($F_{(2, 88)} = 4.86$, $p = 0.01$). Pairwise comparisons revealed that the Frontal group made significantly fewer correct responses than the Controls ($p = 0.007$). There was also a significant Group effect on "Imagined" items misidentified as "Heard" ($F_{(2, 88)} = 6.31$, $p = 0.003$), with pairwise comparisons revealing that the Posterior group made significantly more of these errors than Controls ($p = 0.001$). However there was no significant effect of Group on items incorrectly identified as "New" ($F_{(2, 88)} = 0.92$, $p = 0.40$).

Analysis at the second level revealed the following results

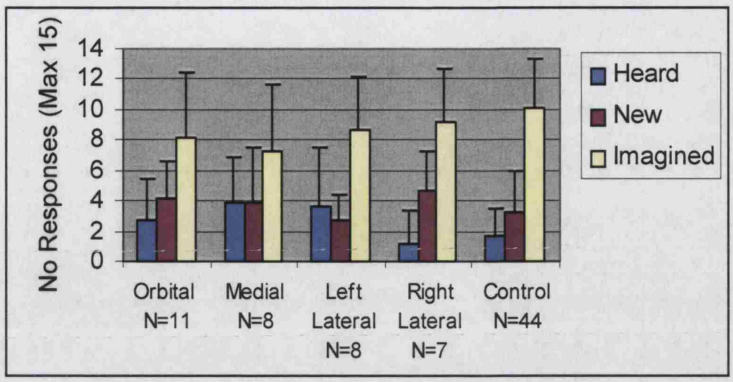

Figure 7.4: Pattern of Responses for Imagined Items by Frontal Subgroup (Grouping / Analysis Level 2)

One-way ANOVAs revealed no significant effect of Frontal Subgroup on correct responses ($F_{(4, 71)} = 2.25$, $p = 0.07$) or on items incorrectly identified as "new" ($F_{(4, 71)} = 0.91$, $p = 0.46$). However there was a significant effect of Frontal Subgroup on items incorrectly identified as "Heard" ($F_{(4, 71)} = 3.11$, $p = 0.02$). Pairwise comparisons revealed that the Medial group made more "Imagined said Heard" errors than the Control group ($p = 0.02$). However given that there was no Frontal effect in the level 1 analysis of this measure a corrected p-level of 0.013 must be employed, and the Medial effect does not reach significance.

Following the significant Frontal effect at Level 1, analysis at level 3 was carried out for correct responses. However no significant effects were found (see Appendix 10 refs 1.1, 2.1, 3.1, 4.1)

New Items:

The pattern of responses for new words (items which had not been previously heard or imagined) is illustrated in figure 7.5.

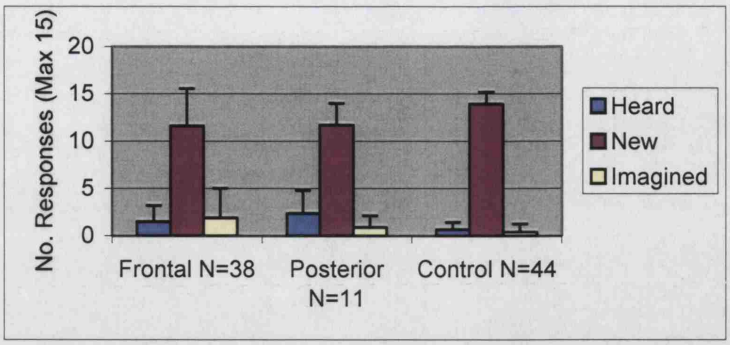

Figure 7.5: Pattern of Responses for New Items by Group

One-way ANOVAs revealed a significant effect of Group on correct responses ($F_{(2, 88)}$ = 8.50, p = 0.000). Pairwise comparisons revealed that both the Frontal (p = 0.000) and Posterior (p = 0.005) groups made significantly fewer correct responses than the Controls. There was also a significant Group effect on "New" items misidentified as "Heard" ($F_{(2, 88)}$ = 5.91, p = 0.004). However Levene's test for equality of error variances was significant ($F_{(2, 90)}$ = 11.55, p = 0.000), and a Kruskal Wallis test failed to confirm the Group effect with a corrected significance level of p = 0.025 (χ^2 = 6.98, df = 2, p = 0.03). Finally there was also a significant effect of Group on items incorrectly identified as "Imagined" ($F_{(2, 88)}$ = 4.93, p = 0.009). Levene's test for equality of error variances was again significant. However a Kruskal Wallis test confirmed the Group effect (χ^2 = 7.86, df = 2, p = 0.02), and pairwise Mann Whitney comparisons revealed that the Frontal group made significantly more of these errors than the Control group (p = 0.006).

Analysis at the second level revealed the following results (Figure 7.6).

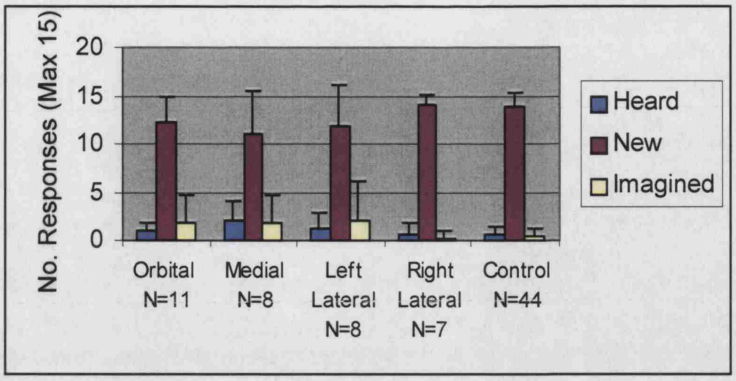

Figure 7.6: Pattern of Responses for New Items by Frontal Subgroup (Grouping / Analysis Level 2)

One-way ANOVAs revealed a significant effect of Frontal Subgroup on correct responses ($F_{(4, 71)} = 3.97$, $p = 0.006$), with pairwise comparisons confirming that the Orbital ($p = 0.01$) and Medial ($p = 0.003$) subgroups made significantly fewer correct responses than Controls. There was also a significant effect of Frontal Subgroup on new items misidentified as "Heard" ($F_{(4, 71)} = 3.20$, $p = 0.02$), with pairwise comparisons revealing that the Medial group made significantly more of this type of error than the Controls ($p = 0.001$). Finally there was also a significant effect of Frontal Subgroup on new items incorrectly identified as "Imagined" ($F_{(4, 71)} = 2.63$, $p = 0.04$). Despite transformation Levene's test for equality of error variances was significant ($F_{(4, 73)} = 4.07$, $p = 0.005$), but a subsequent Kruskal Wallis test confirmed the effect ($\chi^2 = 9.62$, df = 4, $p = 0.05$). Pairwise Mann Whitney U comparisons revealed that the Orbital ($p = 0.04$) and Medial ($p = 0.03$) groups made significantly more of this type of error than Controls.

Following the significant Frontal effects at Level 1, analysis at level 3 was carried out for correct responses, and for New items incorrectly identified as imagined.

Table 7.2:
Mean new items correctly identified: Grouping / Analysis Level 3

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 10.35 (4.36)	N = 11 11.45 (4.34)	N = 13 10.31 (4.96)	N = 11 13.55 (1.81)
Area Not Damaged Mean Score (SD)	N = 19 12.47 (3.53)	N = 25 11.48 (3.98)	N = 23 12.13 (3.35)	N = 25 10.56 (4.41)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the right lateral region identified significantly more new words correctly than those without damage to this area ($t_{(33.95)} = -2.88$, $p = 0.007$).

The data for new items incorrectly identified as imagined can be seen in table 7.3.

Table 7.3:
Mean New items incorrectly identified as imagined: Grouping / Analysis Level 3

	IMOnly	SMIM	LLat	RLat
Area Damaged Mean Score (SD)	N = 17 2.94 (3.75)	N = 11 1.63 (3.04)	N = 13 2.69 (4.07)	N = 11 0.64 (1.29)
Area Not Damaged Mean Score (SD)	N = 19 1.11 (2.40)	N = 25 2.12 (3.32)	N = 23 1.56 (2.61)	N = 25 2.56 (3.62)

Independent samples t-tests for each of the four groupings (comparing those with damage to that particular area to those without damage) revealed that those patients with damage to the right lateral region misidentified significantly fewer of the new words as imagined than those without damage to this area ($t_{(33.20)} = 2.34$, $p = 0.025$).

7.4 DISCUSSION

The reality monitoring task revealed several interesting results regarding the Frontal group's identification of the source of their experiences. Significant comparisons are summarised in table 7.4.

Table 7.4:
Summary of Results: Reality Monitoring Task.

		STIMULUS		
		Heard	Imagined	New
RESPONSE	Heard		Level 1: Posterior Increase Level 2: No effects Level 3: No effects	Level 1: No effects Level 2: Medial Increase Level 3: No effects
	Imagined	Level 1: Frontal Increase Level 2: No effects Level 3: IMonly increase RLat decrease	Level 1: Frontal Decrease Level 2: No effects Level 3: No effects	Level 1: Frontal Increase Level 2: Orbital and Medial Increase Level 3: RLat Decrease
	New			Level 1: Frontal and Posterior Decrease Level 2: Orbital and Medial Decrease Level 3: RLat Increase

Frontal patients (and specifically those with inferior medial damage) were more likely to misidentify words which had been read to them as internally generated, imagined words. Frontal patients were also significantly less likely to correctly identify imagined words. Finally, Frontal patients (and specifically the Orbital and Medial subgroups) were less able to correctly identify new, unpresented words, and were more likely to say that these new words had been imagined. The Medial group were also more likely to misidentify these new words as previously heard.

There are interesting biases therefore among the Medial and Orbital patients to misidentify the source of their experiences. They tend to misidentify new and heard

words as previously imagined. The Medial group in addition misidentify new words as "Heard". In contrast there is no tendency to misidentify words as "New", confirming that the response bias is towards false positive responding (experienced either internally or externally), rather than simple confusion in responding. Those patients with lateral damage, by contrast, seemed preserved on all measures, and those with right lateral damage in particular made less "heard said imagined" errors, identified more new words correctly, and made less "new said imagined" errors.

These results are intriguing when compared to previous neuropsychological and imaging studies of source and reality monitoring. In contrast to the predictions of nearly all of the imaging data that implicated left lateral or bilateral prefrontal regions in source memory, we found no effects of lateral damage in our patients. In fact the right lateral group in level 3 analyses did significantly better than those without right lateral damage. Instead it was the Orbital and Medial groups (and inferior medial at level 3) who differed from normal performance. It is informative to reiterate the areas of frontal damage which were categorised into these groups. The Orbital group comprised patients whose main area of damage was in Brodmann areas 11 and 25. The Medial group had their main area of damage in the region including the following areas: the sub genu (BA 25), the anterior cingulate (BA 23, 24, 32), and the medial surface of the superior frontal gyrus (BA 6, 8 and 10). The inferior medial group at level 3 included all these areas with the exception of the superior frontal gyrus. Anatomically then, the medial results are consistent with the results of Dobbins *et al* (2002) and Simons *et al* (submitted) who both reported medial activation of the superior frontal gyrus or of BA 10 associated with internal context retrieval. The Orbital and Inferior Medial results are less consistent with previous imaging studies of source or reality monitoring, but may also bear some relation to Frith & Frith's (1999) assertion that the ventromedial frontal lobe is particularly involved in reflecting on one's own mental states.

The behavioural features of the Medial and Orbital deficit are consistent with previous reports of an association between frontal lobe damage and high rates of false recognition (Budson *et al*, 2002; Curran *et al*, 1997; Delbecq-Derouesne *et al*, 1990; Melo *et al*,

1999; Parkin *et al*, 1996, 1999; Schacter *et al*, 1996; Swick & Knight, 1999; Verfaillie *et al*, 2004; Ward & Parkin, 2000). There was no consistent bias to misidentify events as externally experienced (heard), which might have been predicted on the basis of past theorising about false recognition and confabulation among frontal patients (e.g. Johnson 1997). However these patients did show a tendency to think that events that had not been experienced had actually been experienced, with the Orbital group tending to attribute them to an internal source (imagined) and the Medial group attributing them to both external (heard) and internal (imagined) sources. There is therefore some evidence of internal / external source confusion amongst a subset of our frontal patients. One reason why more consistent biases were not found may be the heterogeneous nature of our frontal groups. It might be expected that the group most likely to be impaired at reality monitoring, and most likely to exhibit an external source attribution bias, are those patients who confabulate. To investigate this further, the performance of three confabulating patients on this task is analysed separately in chapter 9.

CHAPTER EIGHT:
CONTINUOUS RECOGNITION TASK

8.1 INTRODUCTION

It has frequently been reported that patients with frontal lobe lesions are impaired on temporal memory tasks (e.g. Daum & Mayes, 2000; Milner *et al*, 1985; Shimamura *et al*, 1990; Stanhope *et al*, 1998). Temporal memory has also been implicated in confabulation, with many authors highlighting the fact that events widely separated in time and place become incorrectly fused together or placed in the wrong temporal context. Dalla Barba (1997, 1999) for example, views confabulation as a disturbance of memory and consciousness in which all subjectively experienced temporality is disrupted.

One of the most interesting recent accounts of confabulation and temporality has been provided by Schnider and colleagues (Ptak *et al*, 2001; Ptak & Schnider, 1999; Schnider, 2001; Schnider *et al*, 1996a,b, 2000a,b, 2002; Schnider & Ptak, 1999; Treyer *et al*, 2003). They propose that the critical deficit underlying spontaneous confabulation is an inability to suppress inappropriate associations that do not pertain to ongoing reality. This conclusion is based on the results of a series of experiments using a continuous recognition paradigm in which spontaneous confabulators and non confabulating amnesics were asked to indicate in a long series of pictures those that recurred during the run. After an initial run, subjects were required to complete one or more subsequent runs in which all the items remained the same, but were presented in a different order. A selection of the distractors from the first run now appeared as recurring target items, and the previous targets from the first run were now among the distractors. Thus subjects could not base their responding simply on the familiarity of the items, but had to respond only to items that had appeared already *in the current run.* They found that spontaneous confabulation was consistently associated with "temporal context confusion" (TCC) - a relative increase in false positives in subsequent runs following the first, with subjects falsely alarming to items that should now be ignored. Schnider and colleagues argue therefore that the critical impairment underlying spontaneous confabulation is a failure to

distinguish between currently relevant and currently irrelevant memories, resulting in the erroneous recollection of memory elements that do not belong together. This ability, in contrast to more general temporal memory processes that frontal patients (confabulating and non-confabulating) tend to fail, is argued to be a separate process specifically impaired in spontaneous confabulators.

Schnider and colleagues identified the anterior limbic system, and in particular the medial orbitofrontal cortex (OFC), as critical for suppressing currently irrelevant mental associations of previously encountered info. Damage to the basal forebrain, amygdala and perirhinal cortex, the dorsomedial nucleus or its connections with the OFC in the capsular genu, or the medial hypothalamus and medial orbitofrontal cortex disrupt this ability. This assertion was supported by a PET study in which posterior medial orbitofrontal cortex activation was associated with distinguishing between item repetitions in the present run and previous repetitions from earlier runs (Schnider *et al*, 2000b). This ability should *not* be affected by dorsolateral lesions, which in contrast are associated with failure on more traditional tests of temporal memory that do not distinguish confabulating from non-confabulating patients in both neuropsychological studies (Schacter, 1987; Milner *et al*, 1991; Shimamura *et al*, 1991; Kesner *et al*, 1994; Johnson *et al*, 1997), and imaging studies (Cabeza *et al*, 1997b; Henson *et al*, 1999b; Zorilla *et al*, 1996).

8.2 METHOD

A modified version of the Schnider & Ptak (1999) continuous recognition task was developed in order to explore claims that spontaneous confabulators suffer from an inability to suppress previously relevant but currently irrelevant memory traces. Given that Schnider & Ptak (1999) assume that this confusion of memory traces will be independent of stimulus type, only one version of the task was administered, using landscape scenes as stimuli. These were selected as they are meaningful scenes which are nonetheless difficult to encode verbally.

80 paintings of landscapes were presented one at a time to participants on a computer screen. Each painting appeared for 3 seconds, with a further one-second interval before the next painting appeared. Subjects were instructed to press the space bar on the keyboard every time they saw a painting that they had already seen presented. The 80 stimuli were composed of 50 items: 44 distractors, which appeared once each, and 6 targets, which appeared 6 times each.

Immediately after the first run, a second run was presented. The 80 stimuli were again drawn from the same 50 items, but this time 6 different paintings were selected as the repeating targets, and the previous targets now appeared as distractors. Subjects were told that they were going to see the paintings again, but were instructed to forget that they had seen them all before. They were asked to do the same thing as they had in the first run, and press the space bar when they saw a painting that they had already seen, but only if it was repeated *in the current run.*

30-40 minutes after administration of the first two runs, a third run was presented. Again the 80 stimuli were drawn from the same 50 paintings with a different 6 chosen as targets, and targets from the first 2 runs now appearing as distractors. Subjects were again told that they should forget that they had seen the paintings before and only press the space bar when they saw a picture repeated *in the current run.* The paintings selected as targets in each run, and the order of stimulus presentation within each run, remained constant for all participants.

In the first run familiarity may be used to decide when paintings are repeated. However familiarity will not be an adequate basis for responding in the second and third runs, when all stimuli have been seen before and will therefore be familiar. Correct responding in these runs will depend upon an ability to distinguish between memory traces that are currently relevant, and those that were previously relevant but should now be suppressed. On the basis of previous work (Schnider & Ptak, 1999; Schnider *et al*, 1996b) spontaneous confabulators are expected to produce an increasing number of false positive

responses from runs 1 to 3 compared to other patients and controls, but to show a normal and relatively constant hit rate.

8.3 RESULTS

Performance on the continuous recognition task is presented in table 8.1

Table 8.1:
Performance on the Continuous Recognition Task

		Frontal Mean (SD) N = 39[16]	Posterior Mean (SD) N = 10	Control Mean (SD) N = 48
Run 1	**Hits**	21.82 (9.21)	21.75 (8.58)	27.22 (3.46)
	False Alarms	5.82 (5.34)	6.00 (6.22)	3.74 (4.77)
Run 2	**Hits**	17.28 (8.35)	18.82 (7.92)	23.27 (5.01)
	False Alarms	8.29 (6.70)	7.67 (5.87)	7.58 (5.21)
Run 3	**Hits**	21.54 (7.54)	21.77 (6.10)	25.54 (4.88)
	False Alarms	8.82 (8.47)	7.31 (6.99)	6.14 (5.39)

Hit Rate
The hit rate of the three groups over the three runs is shown in Figure 8.1.

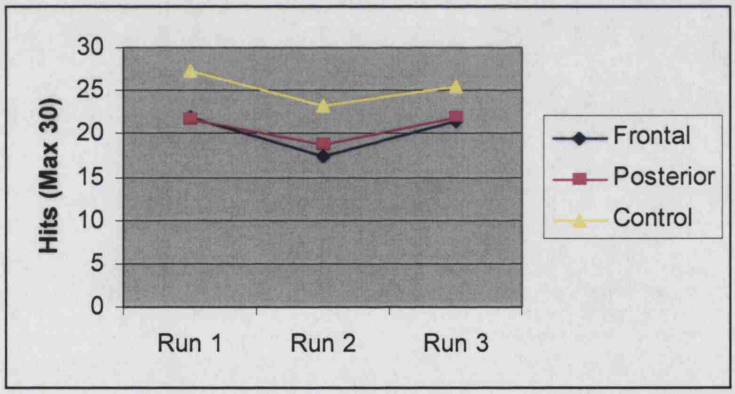

Figure 8.1: Hit Rate (Correct Target Detection)

A mixed model ANOVA on hit rate with Group as the between subjects factor and Run as the within subjects factor revealed no significant effect of Run ($F_{(2, 172)} = 2.33$, $p = 0.10$, Greenhouse Geisser correction), nor a Group x Run interaction ($F_{(4, 172)} = 0.31$, $p = 0.86$, Greenhouse Geisser correction). However there was a significant effect of Group (F

[16] In 6 cases partial data was lost due to technical error. Therefore valid N varies for some runs.

$_{(1, 92)}$ = 11.45, p = 0.000) with a significant covariate of age ($F_{(1, 92)}$ = 19.39, p = 0.000). Levene's test for equality of error variances was significant for hit rates in run 1 ($F_{(2, 94)}$ = 12.70, p = 0.000). However a subsequent Kruskal-Wallis test using combined hit rate across runs confirmed the significance of the group difference (χ^2 = 15.09, df = 2, p = 0.001). Pairwise Mann-Whitney U comparisons confirmed that both the Frontal (U = 520.50, p = 0.000) and the Posterior (U = 118.00, p = 0.012) groups had significantly lower hit rates than the Controls.

Further exploration of whether this deficit might be specific to a particular subgroup of the Frontal patients yielded the following results (Figure 8.2).

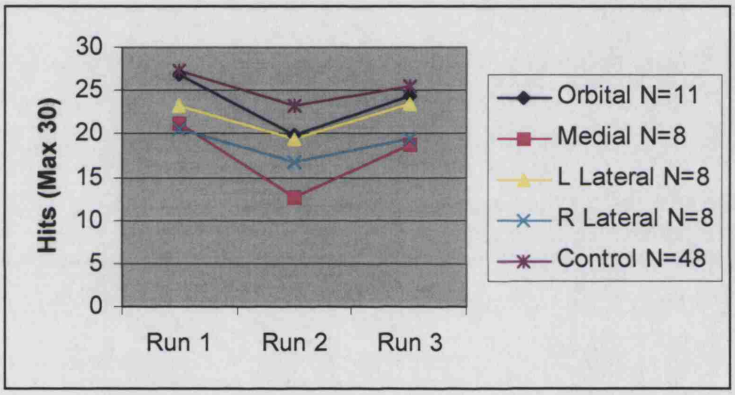

Figure 8.2: Hit rate (Correct Target Detection) by Frontal Subgroup (Grouping / Analysis Level 2)

A mixed model ANOVA on hit rate with Frontal Subgroup as the between subjects factor and Run as the within subjects factor revealed no significant effect of Run ($F_{(2, 152)}$ = 1.55, p = 0.22), nor a Frontal Subgroup x Run interaction ($F_{(8, 152)}$ = 0.54, p = 0.82). However there was a significant effect of Frontal Subgroup ($F_{(4, 76)}$ = 6.95, p = 0.000) with a significant covariate of age ($F_{(1, 76)}$ = 14.64, p = 0.000). Levene's test for equality of error variances was significant for hit rates in run 1 ($F_{(4, 78)}$ = 5.64, p = 0.000). However a subsequent Kruskal-Wallis test using combined hit rate across runs confirmed the significance of the Frontal Subgroup difference (χ^2 = 14.17, df = 4, p = 0.007). Pairwise Mann-Whitney U comparisons confirmed that both the Medial (U = 54.00, p =

0.001) and the R Lateral (U = 102.00, p = 0.04) groups had significantly lower hit rates than the Controls.

Analysis at level 3 revealed no significant lesion group effects (see Appendix 11, refs 1.1, 1.2, 1.3, 1.4)

False Positives

The rate of false positives in each group over the three runs is shown in Figure 8.3

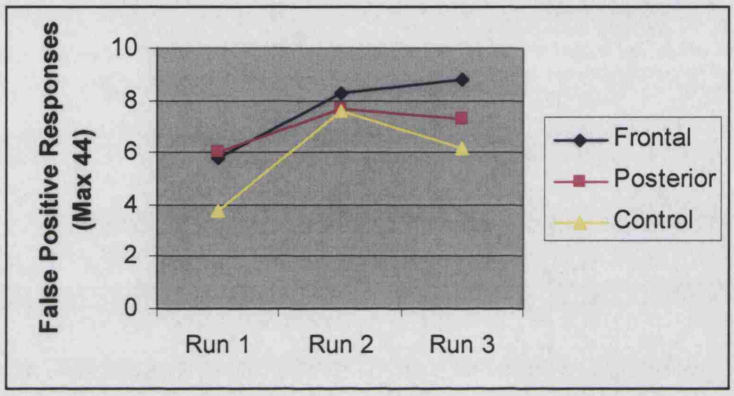

Figure 8.3: False Positive Responses

A mixed model ANOVA with Group as the between subjects factor and Run as the within subjects factor revealed no significant effects (**Run**: $F_{(2, 184)} = 0.12$, $p = 0.89$; **Group**: $F_{(2, 92)} = 0.37$, $p = 0.69$; **Group x Run interaction**: $F_{(4, 184)} = 2.03$, $p = 0.92$).

Analysis at the level of Frontal Subgroup yielded the following results (Figure 8.4).

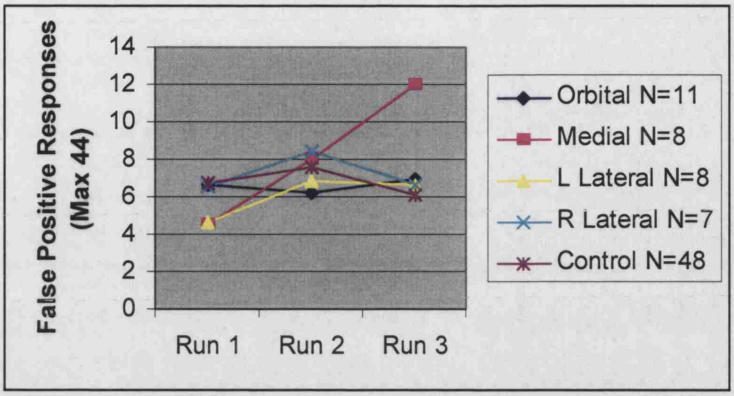

Figure 8.4: False Positive Responses by Frontal Subgroup (Grouping / Analysis Level 2)

A mixed model ANOVA with Frontal Subgroup as the between subjects factor and Run as the within subjects factor revealed no significant effect of Run ($F_{(2, 138)} = 0.17$, $p = 0.83$, Greenhouse Geisser correction), or of Frontal Subgroup ($F_{(4, 75)} = 0.30$, $p = 0.88$). However there was a significant Frontal Subgroup x Run interaction ($F_{(4, 138)} = 2.33$, $p = 0.02$, Greenhouse Geisser correction). It is clear from examination of Figure 8.4 that the interaction arises from the markedly different pattern of false positive responses shown by the Medial group. Most other groups show an interference effect resulting in increased false positives in the second run before dropping back down in run 3. However the Medial group show a steep increase in false positive responses run to run.

To confirm that this pattern was significant, linear trend analyses were carried out for each Frontal Subgroup and for Controls on the rates of false positive responses from run 1 to run 3. This was not significant for the Orbital subgroup ($F_{(1, 10)} = 0.05$, $p = 0.84$), the Left Lateral subgroup ($F_{(1, 7)} = 2.57$, $p = 0.15$), the Right Lateral subgroup ($F_{(1, 6)} = 0.03$, $p = 0.88$) or the Controls ($F_{(1, 47)} = 0.16$, $p = 0.70$). However there was a significant linear trend in the Medial group ($F_{(1, 7)} = 8.92$, $p = 0.02$). Planned comparisons examining Frontal Subgroup differences in hit rates in run 3 confirmed that only the Medial group differed significantly from the Controls ($p = 0.02$)

Analysis at level 3 revealed no significant lesion group effects (see Appendix 11, refs 1.5, 1.6, 1.7, 1.8).

One of the central arguments made by Schnider and colleagues about their continuous recognition task is that it distinguishes confabulating amnesics from non-confabulating amnesics, whilst other tasks have failed to do this. Our Medial group consisted of eight patients, whose individual performance on hit rate and false positives can be seen in figures 8.5 and 8.6.

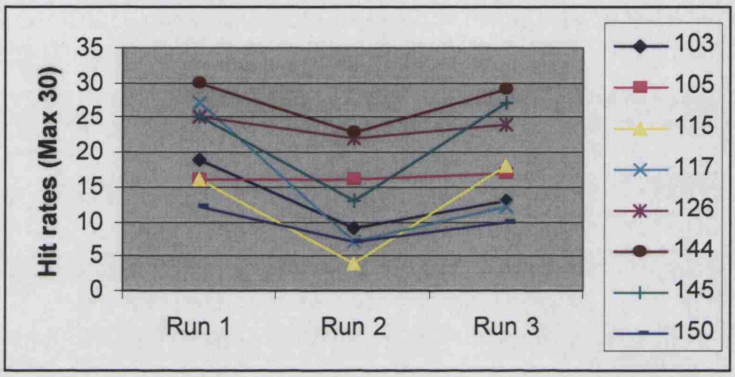

Figure 8.5: Individual hit rates of the eight patients in the Medial group

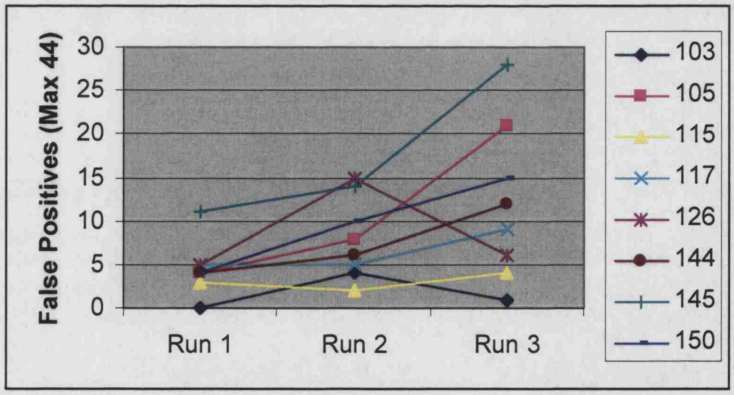

Figure 8.6: Individual false positive rates of the eight patients in the Medial group

Only three of these eight patients were spontaneously confabulating at the time of testing, and those three patients were patients 105, 145 and 150. Strikingly, examination of figure 8.6 suggests that it is indeed these three patients who are driving the Medial effect, each showing a steep increase in false positives from run to run compared to the other patients who show a more stable pattern. Their hit rates however are constant (although patient 145 shows a dip in run 2, his rates at runs 1 and 3 are the same). Moreover their overall hit level is not clearly different from the other five medial patients. Therefore there is no evidence of a general increase in positive responding across runs which might explain the false positive results.

8.4 DISCUSSION

The continuous recognition task revealed that although the Frontal group as a whole (and specifically the Medial and Right Lateral subgroups) had difficulty detecting new target items (as evidenced by their reduced hit rate), the Medial group appeared to show a specific deficit relating to false positives that was not general to the Frontal group. They showed a steep increase in false positive responses from run to run, and were unable to prevent this effect even with an interval of 30-40 minutes between runs 2 and 3. Examination of individual performance within the Medial group revealed that it was the spontaneous confabulators in this group who were driving the effect. As in Schnider & Ptak's (1999) experiment, this increase in false positives cannot be attributed to a general change in response behaviour where patients develop a bias to say "yes", as there was no differential effect on hit rates in these patients. Instead hit rates among all patients showed no significant differences from run to run. It also cannot be explained by a failure to represent new information saliently enough to stop old information intruding into current thinking (Schnider & Ptak, 1999). The Frontal group as a whole did show impaired rates of target detection which might reflect a failure to represent new information saliently, but the false positive pattern was specific only to the Medial group. Moreover the Medial hit rate on run three, where the false positive effect occurred, was virtually equal to that of the Right Lateral group, yet that group showed no increase in false positives.

In terms of neuroanatomy, our results are also consistent with previous findings. Schnider and colleagues identified the anterior limbic system, and in particular the medial orbitofrontal cortex (OFC), as critical for suppressing currently irrelevant mental associations of previously encountered info. In contrast this ability should *not* be affected, they argued, by dorsolateral lesions. Our results are exactly consistent with this hypothesis. Our Medial group comprised patients with damage to regions affecting the anterior limbic system and medial OFC, and we found no effects of lateral lesions on this task.

This pattern of results therefore provides support for the hypothesis of Schnider and colleagues. Schnider *et al* never examined the performance of frontal patients as a group. However with this type of patient the task does indeed appear to distinguish between confabulating and non-confabulating individuals in terms of a distinct pattern in false positive responding[17]. Schnider & Ptak (1999) interpreted this pattern as reflecting a monitoring deficit in which distant mental associations intrude into the present. The fundamental deficit in confabulating patients, they argue, is an inability to suppress mental associations that do not pertain to now. This interpretation is specifically explored in the following chapter.

[17] Note that in the next chapter three other spontaneous confabulators are described whose performance on this task did not apparently fit with this pattern. However further investigation of their deficit indicates they are compatible with this conclusion.

CHAPTER NINE:
SINGLE CASE ANALYSIS OF THREE CONFABULATING PATIENTS: A STUDY OF SCHNIDER'S THEORY OF SPONTANEOUS CONFABULATION

9.1 INTRODUCTION

Confabulation is a specific phenomenon that tends to occur in association with frontal lobe damage, in which false beliefs are held by a patient, often with considerable conviction. They are believed to be true memories and are not intended to deceive the listener. The content of these statements may range from subtle alterations of true events, where real recollections are miscombined or placed in the wrong temporal or other context, to implausible reports of episodes that are bizarre and internally inconsistent. In extreme cases, confabulations may also be associated with an attempt to act upon the mistaken belief. It is frequently accompanied by anosognosia and a lack of awareness of the inaccuracy or absurdity of the beliefs, and the beliefs are often very resistant to contrary evidence.

Many attempts have been made to identify the mechanisms responsible for confabulation, most of which emphasise the role of a frontal or executive impairment in conjunction with an organic amnesia. For example the established link between frontal lobe lesions and impairments in memory for source and temporal information has prompted Johnson and colleagues (e.g. Johnson, 1997; Johnson *et al*, 1997) to highlight the role of deficits in frontally controlled source and reality monitoring processes in confabulation (see also Kopelman *et al* 1997b). Others have focused more exclusively on the temporal memory deficit observed in frontal patients, attributing confabulation to an inability to sequence events temporally, so that events that are related but widely separated in time and place become fused or misattributed to another context. Dalla Barba (1997, 1999) for example views confabulation as a disturbance of memory and consciousness in which all subjectively experienced temporality is disrupted.

Schnider and colleagues' (Ptak *et al*, 2001; Ptak & Schnider, 1999; Schnider, 2001; Schnider *et al*, 1996a,b, 2000a,b, 2002; Schnider & Ptak, 1999; Treyer *et al*, 2003) recent

"temporal context confusion" account of confabulation proposes that the critical deficit underlying spontaneous confabulation is an inability to suppress inappropriate associations that do not pertain to ongoing reality. This conclusion is based on the striking results obtained from their continuous recognition paradigm, in which spontaneous confabulators, as opposed to non confabulating amnesics, show a normal hit rate in combination with a steep increase in false positives from run to run. Spontaneous confabulators in this paradigm seem to be falsely responding to items that are no longer relevant. Schnider and colleagues argued that the critical impairment is a failure to *suppress* activated memory traces that do not pertain to now. Furthermore, they argue that this suppression or deactivation of associations not pertaining to current reality occurs even before they reach consciousness (Schnider, 2001; Schnider *et al*, 2003).

The results of their series of experiments are consistent and striking and have received strong support. Firstly performance on this continuous recognition task, not performance on tests of memory or executive function, exactly parallels the course of spontaneous confabulation (Schnider *et al*, 2000). Secondly PET studies of their task in normal subjects activates the posterior medial OFC, the same area which is damaged in confabulating patients (Schnider *et al*, 2000; Treyer *et al*, 2003). And finally all spontaneous confabulators tested so far have showed this pattern of performance (Schnider *et al*, 1996a, Ptak & Schnider, 1999, Schnider & Ptak, 1999). Indeed the results presented in the previous chapter provide the first replication of the temporal context confusion effect from a research team other than Schnider's.

The pattern of performance associated with spontaneous confabulation, and the involvement of the posterior medial OFC is therefore reliably supported. However the mechanism proposed to underly both the increase in false positives in the continuous recognition task, and to underly spontaneous confabulation itself, has not been subject to explicit experimental testing. Schnider and colleagues argue that the critical impairment is a failure to *suppress* activated memory traces that do not pertain to "now" (e.g. Schnider & Ptak, 1999). In an attempt to explicitly test this hypothesis we examined the performance of three spontaneously confabulating patients, selected from the series, on

the original continuous recognition task used by Schnider and colleagues, and on two newly developed temporal discrimination tasks that assessed the temporal memory abilities of our confabulating patients, and enabled an examination of whether previously experienced items intruded into the present for these patients, therefore needing to be suppressed.

9.2 CASE REPORTS

Three male patients with clear and ongoing confabulatory disorders were selected from the series. Each of the patients confabulated spontaneously on a regular basis, and a feature of the confabulation in each case was a tendency to attempt to act upon the incorrect beliefs. Individual features are described below[18].

Patient 123

Patient 123 was a 53 year old right handed man. He was a university graduate who had previously run a successful business. He was admitted to Aberdeen Royal Infirmary in September 2001 with a grade 2 subarachnoid haemorrhage. Angiogram showed an anterior communicating artery aneurysm that was clipped on 18th September 2001 leaving him with persistent confusion and memory impairment with confabulation. Neurological examination was normal.

Patient 123 was seen on three occasions in February 2002, May 2002 and September 2002. The content and frequency of his confabulation had improved markedly in the period between his hospital admission and research assessment as his awareness of his memory impairment increased. He was the least severe confabulator of the three, and as he became more aware of his confabulation he was learning to say he did not know things rather than to offer an answer that might be incorrect. However he was still confabulating and attempting to act on his false beliefs throughout the eight month course of the

[18] Two of these patients (131 and 143) were amongst the 8 confabulating patients identified in performance-led analysis of the Confabulation Battery in Chapter 4, but none of them were amongst the 3 identified in analysis of the continuous recognition task in Chapter 8. These patients were selected for follow up because of the ongoing nature of their confabulation, and their availability for testing.

research assessment. By this time his confabulations no longer had any bizarre content but centred around his everyday tasks. He confabulated about things he had done earlier that day or that week, for example believing that he had been on his farm (which was his normal routine) when he had not. His wife commented that although he had previously run a successful business with her, he was no longer able to assist her as he would repeatedly attempt to carry out tasks that he had already completed.

Examination of MRI showed some swelling of the left hemisphere with lesions in the left orbital region laterally. Scan artefacts made it difficult to draw conclusions about the specific regions of damage but there was some indication of a possible lesion below the head of the caudate, possibly including the nucleus accumbens. The septal nuclei were thought not to be affected. In the main series he was allocated by the consultant radiologist to the "Orbital" group.

Patient 131

Patient 131 was a 59 year old right handed man who was referred to the National Hospital for Neurology and Neurosurgery in April 2002 after he was found disoriented in the street. His occupation prior to his illness was a chef, but details of his schooling are unknown. Investigations revealed no evidence of current illness and neurological examination was normal, but CT showed previous frontal lobe surgery and a shunt. Patient 131 reported that he had had a tumour removed 2-3 years previously.

When his notes were traced it was revealed that he had actually suffered a sub-arachnoid haemorrhage and undergone a left frontal craniotomy and clipping of a large anterior communicating artery aneurysm in November 1977. Postoperatively he had remained in a profound confusional state with poor memory. In March 1978 a right ventricular arterial shunt was inserted. He attempted to return to work in November 1978 but was unable to hold down a job and was admitted to a rehabilitation service for two months until May 1979. Following the death of his mother in December 1983 he was admitted to a psychiatric unit in May 1984 where they had been working towards adult fostering but he walked out in July 1984. It appears that he lived with his brother until 1986. Between

1986 and 2002 his living arrangements are unknown but he spent at least part if not all of this time on the streets. During this period he was admitted to various London hospitals after being found on the streets with confusion and memory problems. On at least one occasion he underwent psychiatric assessment where his memory and orientation problems were noted but he was found to have no psychiatric symptoms. There was no evidence of any history of alcohol abuse, Patient 131 stated that he did not drink at all, and his carers in the placement found for him following his admission at NHNN confirmed this.

Patient 131 was seen as part of the current research project in April 2002, and again in September 2002. Even 25 years after his aneurysm rupture he continued to confabulate about the history of his illness and his family history, most frequently mistaking the time since events had happened. For example he continued to insist that he had undergone surgery 18 months to 2 years previously and that he had stopped work as a chef two and a half years previously when he was sacked for forgetting to turn the steamers off. He said that he had met the examiner 8 weeks ago when he had actually met her only a few days previously. He was very aware that his memory was bad and frequently referred to this in conversation, saying that he had suffered memory problems since his wife left him which he thought was in 2000 (actually 1978). He also described several events that seemed bizarre in content and are likely to have been confabulatory. For example he described in great detail a holiday he had taken his mother on at the request of her surgeon, when he was allowed into the cockpit to see the pilot land the plane. Patient 131 would also confuse the source of his memories, for example telling the examiner that another male patient on the ward had had a laptop which played music when it started up, when actually this memory referred to an earlier testing session with her. On occasion he would attempt to act on his incorrect beliefs, and frequently attempted to leave the hospital. On one occasion after being missing for 24 hours he presented to Barts Hospital (where he had been in 1977) believing that he was still a patient there.

Examination of his CT scan revealed a substantial deficit involving a number of regions. There was involvement of the orbital region bilaterally but mainly on the left, and also

involvement of the sub genu on both sides. The anterior aspect of the anterior cingulate was also affected, again on the left more than the right. The left anterior superior frontal gyrus was involved on the medial and lateral surfaces, and a little bit of the convexity. Superior frontal gyrus damage was also present to a much lesser degree on the right where the deficit appeared to be mainly within the white matter. Detailed conclusions were made difficult by the lack of MRI but there was probable involvement of the diagonal band of Broca and septal nuclei. In the main series he was not placed in a level 2 group as his lesion was too extensive to be classified into just one area

Patient 143

Patient 143 was a 64 year old right handed man who had previously worked as journalist. He had a degree in English and a postgraduate qualification in journalism. He suffered a subarachnoid haemorrhage whilst on holiday on 26th July 2002. He was transferred to the National Hospital where an angiogram showed a ruptured left anterior communicating artery aneurysm and an unruptured right posterior communicating artery aneurysm. He underwent left pterional craniotomy and wrapping of the left anterior communicating artery aneurysm on 29th July 2002. Post operatively he made a good physical recovery but suffered significant problems with memory, attention and confabulation and was admitted to the Acute Brain Injury unit. Neurological examination was normal, and he was seen as part of the current research project between 22nd August and 5 December 2002.

He remained disoriented and confabulatory throughout his stay in the hospital. He was disoriented in time, believing that the year was 1972 and that he was in a navy hospital in South Africa after having been injured by aerial fire whilst boarding a ship. His confabulations were constant; indeed it was difficult to interrupt the flow of his confabulatory conversation. He often believed himself to be in a foreign country in war time. Whilst these confabulations were often based on past occupational experiences and countries he had lived in, the content of other confabulations was more bizarre. For example whilst looking for his socks he told the examiner that life insurance policies had recently been adjusted according to whether the applicant had recently bought socks or

not, as buying socks implied that they would probably be around for a while. On another occasion he told the examiner about a party he had recently attended where he had met the mother of a friend of his who had the head of a bee. Although his confabulations could nearly always be traced back to some thought or event (for example he had ptosis of the left eye which he had attributed to a bee sting shortly before his confabulation about the party) they were clearly more unusual than confabulations which could be described as being correct but simply currently irrelevant. He frequently attempted to act upon his incorrect beliefs, trying to leave the hospital to attend meetings or to drive into war zones, or leaving the testing room to check that his food was not burning. Whilst the degree of his confabulation did lessen somewhat over the period of the research, he remained a florid confabulator by December 2002, particularly when tired or feeling under pressure. For example when last seen he claimed that he had attended the examiner's wedding a few weeks previously, and had just returned from France where he had bought a house.

Examination of his MRI scan revealed involvement both of the orbital surface (mainly on the right but also on the left), and of bilateral medial regions. In the main series he was placed in the Orbital group.

Controls:
For tests that were conducted as part of the main series, these patients were compared both to the Control sample of the series described previously, and to the Frontal group (with these three excluded). For the new experimental tests five non-brain-damaged male controls matched for age with the three patients were recruited.

9.3 NEUROPSYCHOLOGICAL ASSESSMENT

The baseline neuropsychological results for the three patients can be seen in table 9.1.

Table 9.1:
Baseline neuropsychological assessment of the three spontaneously confabulating patients.

IQ, Naming and Perception	Patient 123	Patient 131	Patient 143
NART Estimated Premorbid IQ	121	105	101
Ravens APM	9 (66 %ile)	7 (72 %ile)	8 (84 %ile)
Graded Naming Test Scaled Score	22/30 (50-75 %ile)	23/30 (75 %ile)	19/30 (25-50 %ile)
Fragmented Letters	20/20	20/20	20/20
Executive Functions			
FAS Verbal Fluency	27 (<10%ile)	29 (10-20%ile)	28 (10-20%ile)
Stroop	70/112 (14-16%ile)	84/112 (24%ile)	54/112 (2-4%ile)
Trails A Time to complete (s)	40 (20-30%ile)	51 (25-50%ile)	57 (<10%ile)
Trails B Time to complete (s)	70 (50-60%ile)	162 (10%ile)	134 (<10%ile)
WCST	6 categories, 3 errors (0% perseverative)	6 categories, 28 errors (54% perseverative)	6 cats, 14 errors (21% perseverative)
Cognitive Estimates	0 (95 %ile)	5 (25 %ile)	8 (1 %ile)
Hayling	3 (Poor)	4 (Low Average)	3 (Poor)
Brixton	6 (Average)	2 (Abnormal)	6 (Average)
Memory			
Rey Copy Score	35/36 (85 %ile)	33/36 (69 %ile)	36/36 (89 %ile)
Rey 40 minute Delayed Recall	12/36 (34 %ile)	8.5/36 (18 %ile)	0/36 (<5 %ile)
RMT Words	38/50 (10-25 %ile)	38/50 (10-25%ile)	29/50 (< 5%ile)
RMT Faces	42/50 (25-50%ile)	26/50 (<5%ile)	28/50 (<5%ile)
Doors and People			
Visual Memory Score	6 (10%ile)	-	-
Verbal Memory Score	7 (10-25%ile)	-	5 (5%ile)
Recall Score	5 (5%ile)	-	-
Recognition Score	7 (10-25%ile)	-	6 (5-10%ile)
Verbal Forgetting Score	6 (10%ile)	-	7 (25%ile)
Visual Forgetting Score	4 (1-5%ile)	10 (5%ile)	-
AMIPB Story Recall			
Immediate Recall	19/56 (10-25%ile)	17/56 (10-25%ile)	3/56 (5%ile)
	3 intrusions	0 intrusions	5 intrusions
Delayed Recall	1/56 (<10%ile)	8/56 (<1%ile)	0/56 (< 1%ile)
	3 intrusions	2 intrusions	8 intrusions
RBMT Story Recall			
Story 1 Immediate Recall	7/21 (24 %ile)	3.5/21 (5 %ile)	2.5/21 (< 5 %ile)
	1 intrusion	2 intrusions	10 intrusions
Story 1 Delayed Recall	0/21 (< 5 %ile)	0/21 (< 5 %ile)	0.5/21 (< 5 %ile)
	1 intrusion	1 intrusion	5 intrusions
Story 2 Immediate Recall	7/21 (24 %ile)	4.5/21 (9 %ile)	0/21 (< 5 %ile)
	0 intrusions	0 intrusions	6 intrusions
Story 2 Delayed Recall	0/21 (< 5 %ile)	0/21 (< 5 %ile)	0/21 (< 5 %ile)
	2 intrusions	0 intrusions	6 intrusions
Story 3 Immediate Recall	3/21 (< 5 %ile)	4.5/21 (9 %ile)	5/21 (12 %ile)
	0 intrusions	1 intrusion	3 intrusions
Story 3 Delayed Recall	0/21 (< 5 %ile)	0/21 (< 5 %ile)	1/21 (< 5 %ile)
	0 intrusions	0 intrusions	0 intrusions
Story 4 Immediate Recall	9.5/21 (47 %ile)	7/21 (24 %ile)	5/21 (12 %ile)
	0 intrusions	1 intrusion	2 intrusions

Story 4 Delayed Recall	0/21 (< 5 %ile) 0 intrusions	6.5/21 (30 %ile) 1 intrusion	0/21 (< 5 %ile) 0 intrusions
RAVLT			
Total Recall A Trials 1-5	51 (73 %ile)	26 (<5 %ile)	29 (19 %ile)
Recall List B	7 (81 %ile)	4 (22 % ile) (2 intrusions)	4 (32 %ile)
Recall A Trial 6	2 (< 5 %ile)	2 (< 5 %ile) (3 intrusions)	0 (< 5 %ile)
Delayed Recall	1 (< 5 %ile)	1 (< 5 %ile) (8 intrusions)	1 (< 5 %ile) (1 intrusion)
Recognition List A / 15	8 (10 %ile)	10 (30 %ile)	11 (61 %ile)
Recognition List B / 15	5 (49 %ile)	2 (19 %ile)	4 (52 %ile)

* Percentiles compared with published norms.

Intellectual functioning (as measured by Ravens APM), naming skills, and perception were preserved in all three patients. Executive functions were in general at the low end of the normal range with considerable variation between tests. There was no one test that all patients failed, nor was there any patient who failed all executive function tests. Memory performance also did not show any consistent patterns across the patients. Recognition skills (as assessed by the RMT, Doors and People recognition scale, and recognition subtest of the RAVLT) were preserved in patient 123, and mixed in patients 131 and 143, with both showing a recognition deficit for visual but not verbal stimuli in the RMT, and a deficit in the Doors and People, but preserved performance on recognition in the RAVLT. Recall performance was more consistently impaired. With the exception of the Rey Complex Figure Test, in which patients 123 and 131 performed well, all three patients were impaired in recall tasks, for instance on the Doors and People and Delayed Story Recall. A particular feature of the recall of all three patients was a tendency to produce intrusions in their recall, and each of them also showed a susceptibility to retroactive interference as evidenced by recall of list A in the RAVLT following recall of list B.

9.4 BATTERY PERFORMANCE

The performance of the three confabulating patients on the new experimental tests administered to the whole frontal series is presented below. They are compared to the series Control group and to the series Frontal group (with the data of these three patients excluded).

9.4.1 Confabulation Battery:

Table 9.2 shows the performance of the three confabulating patients on the confabulation battery described in Chapter 4.

Table 9.2:
Confabulation Battery: Performance of three single cases

	123	131	143	Frontal	Control
Valid N	1	1	1	35	50
Total Confabulations	2*	7*	16*	1.46 (1.72)	0.58 (0.64)
General Semantic Memory Questions (Maximum 5):					
Mean Correct Responses	5	4	3*	4.83 (0.57)	4.80 (0.49)
Mean "Don't Know" Responses	0	0	0	0.09 (0.28)	0.10 (0.36)
Mean Confabulations	0	1*	2*	0.09 (0.37)	0.10 (0.36)
Personal Semantic Memory Questions (Maximum 5):					
Mean Correct Responses	5	5	3*	4.91 (0.28)	4.98 (0.14)
Mean "Don't Know" Responses	0	0	0	0.00 (0.00)	0.02 (0.14)
Mean Confabulations	0	0	2	0.09 (0.28)	0.00 (0.00)
Personal Episodic Memory Questions (Maximum 5):					
Mean Correct Responses	2	2	1	4.66 (0.73)	5.00 (0.00)
Mean "Don't Know" Responses	2	1	0	0.06 (0.24)	0.00 (0.00)
Mean Confabulations	1	2	4	0.29 (0.62)	0.00 (0.00)
Orientation In Time Questions (Maximum 5):					
Mean Correct Responses	4*	4*	2*	4.69 (0.53)	4.90 (0.36)
Mean "Don't Know" Responses	1	0	0	0.00 (0.00)	0.00 (0.00)
Mean Confabulations	0	1*	3*	0.31 (0.53)	0.10 (0.36)
Orientation in Place Questions (Maximum 5):					
Mean Correct Responses	5	3*	1*	4.60 (0.65)	4.80 (0.40)
Mean "Don't Know" Responses	0	0	0	0.09	0.08

				(0.28)	(0.27)
Mean Confabulations	0	2*	4*	0.31 (0.58)	0.12 (0.33)
"Don't Know" Questions (Maximum 5):					
Mean Correct Responses	0	0	0	0.17 (0.38)	0.22 (0.42)
Mean "Don't Know" Responses	5	5	4	4.63 (0.55)	4.62 (0.49)
Mean Confabulations	0	0	1*	0.20 (0.41)	0.16 (0.37)
Little Red Riding Hood Story (Maximum 1):					
Mean Correct Responses	0	0	0	0.66 (0.48)	0.74 (0.44)
Mean "Don't Know" Responses	0	0	0	0.17 (0.38)	0.16 (0.37)
Mean Confabulations	1*	1*	1*	0.17 (0.38)	0.10 (0.30)

* indicates performance > 2 SD outside the normal range

Examination of table 9.2 confirms that patient 123 is the mildest confabulator of the three, and reflects the fact that by the time of testing he was beginning to learn to control his confabulatory tendencies, particularly in a controlled testing situation. Patient 131 produces more confabulations, but like patient 123, and consistent with the majority of previous reports (Dalla Barba *et al*, 1990; 1997; Dalla Barba 1993a,b; Nedjam *et al*, 2000), these tend to be restricted to episodic or orientation questions. Patient 143 on the other hand is the most severely affected, confabulating in response to every category of question, including those in the semantic domain. This is not surprising given the content of his day-to-day confabulations, which were sometimes so bizarre that they were semantic confabulations by definition.

9.4.2 Verbal Organisation and Monitoring Task:

Table 9.3 shows the performance of the three confabulating patients on the verbal OM task described in Chapter 5.

Table 9.3:
Verbal OM Task: Performance of three single cases

	123	131	143	Frontal	Control
N	1	1	1	34	50
Mean Correct Recalls per list (Max 16)	3.83*	3.17*	1.00*	7.34 (3.41)	9.84 (2.59)
Blocked Lists	4.67*	4.33*	0.33*	7.69 (3.71)	10.44 (2.38)
Random Lists	3.00*	2.00*	1.67*	6.85 (3.34)	9.25 (3.11)
Mean No. Categories Recalled per List (Max 4)	1.83*	1.33*	0.67*	2.95 (0.91)	3.57 (0.38)
Blocked Lists	1.67*	1.67*	0.33*	2.95 (0.88)	3.57 (0.43)
Random Lists	2.00*	1.00*	1.00*	2.95 (1.01)	3.57 (0.43)
Mean No Words Recalled per Category (Max 4)	2.00	2.61	1.33*	2.41 (0.53)	2.73 (0.54)
Blocked Lists	2.50	3.22	1.00*	2.54 (0.59)	2.92 (0.49)
Random Lists	1.50	2.00	1.50	2.28 (0.58)	2.55 (0.68)
Mean No. Unnecessary Category Switches per List	0.17	0.17	0.00	0.43 (0.54)	0.55 (0.44)
Blocked Lists	0.00	0.33	0.00	0.26 (0.53)	0.36 (0.39)
Random Lists	0.33	0.00	0.00	0.61 (0.68)	0.74 (0.69)
Mean Extra-List Intrusions per list	0.33	2.00*	0.67	0.42 (0.43)	0.36 (0.41)
Blocked Lists	0.67	2.33*	0.67	0.58 (0.65)	0.50 (0.71)
Random Lists	0.00	1.67*	0.67	0.26 (0.34)	0.23 (0.30)
Mean Prior-list Intrusions per list	0.00	0.60	0.00	0.63 (0.76)	0.60 (0.59)
Blocked Lists	0.00	1.00	0.00	0.81 (1.26)	0.73 (0.84)
Random Lists	0.00	0.33	0.00	0.52 (0.59)	0.51 (0.68)
Following Prompting:					
Mean Additional Correct Responses Following Prompting	2.83	6.50*	6.17*	1.96 (1.17)	1.45 (0.89)
Blocked Lists	3.00	5.33*	7.33*	2.10 (1.51)	1.44 (1.17)
Random Lists	2.67	7.67*	5.00*	1.82 (1.19)	1.47 (1.16)
Mean Additional Extra-List Intrusions Following Prompting	1.83*	7.50*	3.50*	0.56 (0.77)	0.25 (0.30)
Blocked Lists	1.67*	7.33*	5.33*	0.60 (0.84)	0.24 (0.36)
Random Lists	2.00*	7.67*	1.67*	0.53 (0.83)	0.26 (0.45)
Mean Additional Prior-list intrusions Following Prompting	0.00	1.40*	1.20*	0.29 (0.37)	0.12 (0.20)
Blocked Lists	0.00	1.00*	1.50*	0.29 (0.43)	0.10 (0.25)
Random Lists	0.00	1.67*	1.00*	0.27 (0.47)	0.13 (0.26)
Monitoring:					
Percentage Words Correctly Monitored	100.00%	85.42%	79.17%	89.29 % (12.05)	88.78 % (10.42)
Percentage Words Incorrectly Identified as Repeated	16.67%	37.68%*	89.29%*	7.00% (9.41)	5.00 % (9.41)

* indicates performance > 2 SD outside the normal range

All three patients have correct recall rates in the verbal OM task that are significantly below normal. It appears that this is because they are losing entire categories of words, as the number of words they recall within a category when it is remembered is well within the normal range (except for patient 143). Patient 131 especially also produces very high rates of extra-list intrusions in his recall. None of the patients make high numbers of unnecessary category switches in their recall, which would indicate a generally disorganised recall strategy. However they do benefit from category prompting at recall, which greatly increases their correct recall rates. This fits with the suggestion that whilst they lose entire categories of words, when they do remember these categories they are able to produce a normal number of words for each one. However prompting has the unwanted effect of leading to greatly increased rates of extra-list intrusions too. Their rates of correct monitoring of words which have been previously presented are good. However they are overinclusive in their monitoring, and have a tendency to incorrectly identify words as repeated as well.

9.4.3 Visual Organisation and Monitoring Task:

Table 9.4 shows the performance of the three confabulating patients on the visual OM task described in Chapter 5.

Table 9.4:
Visual OM Task: Performance of three single cases

	123	131	143	Frontal	Control
N	1	1	1	37	50
Mean Correct Recalls per Picture (Max 10)	5.25	4.50*	2.75*	5.57 (1.61)	6.66 (1.07)
Organised Pictures	7.50	4.25*	2.50*	5.98 (1.83)	6.89 (1.24)
Random Pictures	3.00*	4.75	3.00*	5.17 (1.66)	6.43 (1.11)
Mean Extra-Picture Intrusions per Picture	0.38*	0.38*	1.50*	0.12 (0.16)	0.06 (0.10)
Organised Pictures	0.50*	0.50*	1.75*	0.07 (0.15)	0.08 (0.13)
Random Pictures	0.25	0.25	1.25*	0.17 (0.27)	0.05 (0.13)
Mean Prior-Picture Intrusions per Picture	0.50	0.33	0.67	0.53 (0.45)	0.39 (0.35)
Organised Pictures	0.67	0.33	0.67	0.51 (0.58)	0.43 (0.42)
Random Pictures	0.33	0.33	0.67	0.51 (0.57)	0.32 (0.40)
Percentage Images Correctly Monitored	97.22%	66.67%*	100.00%	93.29% (7.64)	92.89 % (8.57)
Percentage Images Incorrectly Identified as Repeated	12.50%	0.00%	25.00%	17.90% (22.04)	10.96 % (15.11)

In the visual OM task the correct recall of patients 123 and 131 is better than in the verbal OM task, but patient 143's recall is again reduced. All three have much higher rates of extra-picture intrusions than normal controls, although their rates of prior-picture intrusions are normal. The fact that prior-list and prior-picture intrusions are normal in both the visual and verbal OM tasks is interesting as temporal confusion accounts of confabulation, and Schnider and colleagues' account of confabulation, would predict that most errors should arise from real events that have been temporally displaced. Instead the intrusions that these patients are making are of non-presented items. Monitoring performance is reduced in patient 131, but is normal in patients 123 and 143.

9.4.5 Encoding Specificity Task:

Table 9.5 shows the performance of the three confabulating patients on the encoding specificity task described in Chapter 6.

Table 9.5:
Encoding Specificity Task: Performance of three single cases

	123	**131**	**143**	**Frontal**	**Control**
N	1	1	1	37	50
SPECIFIC DIMENSION					
Actual Correct Encoding	9.00*	11.00	13.00	10.49 (4.57)	13.40 (2.10)
Raw Recall (Max 15)	5.00	1.00*	0.00*	8.41 (3.91)	10.88 (2.95)
Actual Corrected Recall Given Correct Encoding (%)	56.00	0.00*	0.00*	61.00 (32.00)	73.00 (20.00)
Intrusions (%)	8.33	76.92*	50.00*	14.65 (14.85)	12.28 (9.16)
Incorrect alternative	0.00	7.69*	7.14*	0.97 (2.51)	0.62 (2.13)
Previous item	8.33	7.69	21.43	8.37 (8.66)	9.68 (7.20)
New word	0.00	61.54*	21.43*	5.31 (9.55)	1.98 (4.23)
Don't Know (%)	50.00*	23.08	50.00*	26.83 (22.60)	15.11 (15.58)
SIMILAR CONDITION					
Actual Correct Encoding	15.00	13.67	4.34*	12.61 (4.08)	14.36 (1.02)
Raw recall (Max 15)	2.00	0.00*	0.00*	4.57 (2.78)	6.48 (2.83)
Actual Corrected Recall Given Correct Encoding (%)	13.00	0.00*	0.00*	31.00 (22.00)	42.00 (20.00)
Intrusions (%)	13.33	71.43*	28.57	29.24 (18.08)	19.67 (12.35)
Incorrect alternative	0.00	0.00	0.00	0.21 (1.26)	1.0 (0.00)
Previous item	13.33	7.14	0.00	20.83 (14.54)	16.35 (11.31)
New word	0.00	64.29*	28.57*	8.21 (12.53)	3.32 (5.70)
Don't Know (%)	73.33	28.57	71.43	40.01 (20.18)	38.04 (18.80)

* indicates performance > 2 SD outside the normal range

In general correct encoding rates are comparable to the Frontal and Control groups. Patients 143 has a marked drop in correct encoding in the similar condition, but without replication it would be inappropriate to draw any conclusions from this. All three patients however have reduced raw and corrected recall rates, and patients 131 and 143 recalled almost nothing. These two patients instead have very high rates of intrusions in their recall, and in particular very high rates of new word intrusions (reminiscent of the high rates of extra-list and extra-picture intrusions in the visual and verbal OM tasks). Patient 131 in particular produces large numbers of new non-presented words – in the similar condition these account for 64 % of his recall.

9.4.6 Continuous Recognition Task (Battery Version):

Table 9.6 shows the performance of the three confabulating patients on the continuous recognition task described in Chapter 8.

Table 9.6:
Continuous Recognition Task: Performance of three single cases

		123	131	143	Frontal Mean (SD) N = 36	Control Mean (SD) N = 48
Run 1	Hits	28	9	29	21.81 (9.21)	27.22 (3.46)
	False Alarms	4	5	15	5.64 (5.33)	3.74 (4.77)
Run 2	Hits	21	14	-	17.75 (8.14)	23.27 (5.01)
	False Alarms	5	13	-	8.49 (6.77)	7.58 (5.21)
Run 3	Hits	23	25	17	21.53 (7.80)	25.54 (4.88)
	False Alarms	8	18	6	8.67 (8.68)	6.14 (5.39)

The three patients each appear to show rather different patterns in performance on the continuous recognition task. Patient 123's performance is largely similar to controls. He has a fairly high, constant hit rate run to run, and fairly low rates of false positives. He does not show the steep increase in false positive responding associated with spontaneous confabulation by Schnider and colleagues (e.g. Schnider & Ptak, 1999), or in the results reported in chapter 8. Patient 131 on the other hand shows this increase in false positive responding very clearly. However his hit rate starts low in the first run and then increases in runs 2 and 3. This indicates poor target detection followed by an increasing bias to

respond positively, which could account for his false positive responding rate. Patient 131 therefore does not fit the predictions made by Schnider & Ptak (1999) and by the findings in chapter 8 either. Finally patient 143's data is difficult to evaluate due to technical faults that meant that data about his performance in run 2 was lost. However comparing his performance in run 1 and run 3 reveals a drop in both false positive rate and hit rate. His results again do not fit with predictions.

The reasons for this unexpected failure to replicate Schnider & Ptak's results, and our own results in chapter 8, are likely to be to do with task differences between our continuous recognition test, and that employed by Schnider & Ptak (1999). In Schnider & Ptak's original task there were only 4 targets which were presented 8 times each (in a series of 80 items). In our version there were 6 targets which appeared 6 times each (again in a series of 80 items). We also used landscape pictures which are more similar and more easily confusable than Schnider & Ptak's objects and geometric designs. It appears that the increased difficulty of our task may have reduced our patients' hit rates and prevented traces of the previous targets from becoming strong enough to intrude into future runs. The task is obviously capable of creating the effect reported by Schnider & Ptak, as the results in Chapter 8 demonstrate. One possibility is that it may be too difficult to reproduce the Schnider & Ptak effect in all confabulating patients, particularly those who are suffering more marked memory problems such as those described here. Alternatively however it may be that our three confabulating patients actually do not show the temporal confusion effect that Schnider & Ptak predict they should. In order to decide between these two possibilities, the original Schnider & Ptak task was obtained and run with the three confabulating patients. The results of this are reported below.

9.5 SCHNIDER & PTAK (1999) ORIGINAL CONTINUOUS RECOGNITION TASK

Design and Procedure:

In an attempt to replicate Schnider and colleagues' results, we administered their original continuous recognition task (Schnider & Ptak, 1999) to our 3 spontaneous confabulating

patients. We administered both versions of the task, first with meaningful figures as stimuli, and then with nonsense geometric designs. The design and procedure were as described in Schnider & Ptak (1999) as follows:

> "In all runs, 80 items drawn from a constant set of 52 items were presented. Unknown to the subjects, a series of 80 items was composed of 8 groups of 10 items each. Four of these 10 items were present in all eight groups and thus recurred seven times after initial presentation (28 targets); the other six items would not recur (52 distracters). Subjects were required to indicate item recurrences. All items were presented on a computer screen for 2000 ms. The test subjects responses were types in by the examiner.... Target items were different in each run: the four target items from one run were among the distracters in all subsequent runs, whereas four previous distracters were randomly selected as the target items of the next run. The distribution of target items within each group of ten items and the order and distribution of all distracters were randomized in each run. Immediately after the first run a second run was made. Subjects were asked to forget that they had just seen all items and that they should indicate item recurrences only within this second run. During the run, the question "Have you seen this picture in this very run yet?" was repeated several times. Five minutes after the second run the third run was made. Thirty minutes after the third run the fourth run was made" (p680)

Results:

Figures 9.1 and 9.2 show the performance of our three patients along with the performance of the spontaneous confabulator, provoked confabulator and control groups from Schnider & Ptak's (1999) original study[19].

Figure 9.1 illustrates that whilst the hit rates of confabulating and nonconfabulating patients remain relatively stable across runs, the spontaneous confabulators in the Schnider & Ptak 1999) study, and the three confabulating patients presented here can be distinguished by a steep increase in false positives from run to run. Although this pattern is less marked in the nonsense designs version of the task (patient

[19] Figures presented for the Schnider & Ptak (1999) data are estimated from their graphs as raw data were not provided

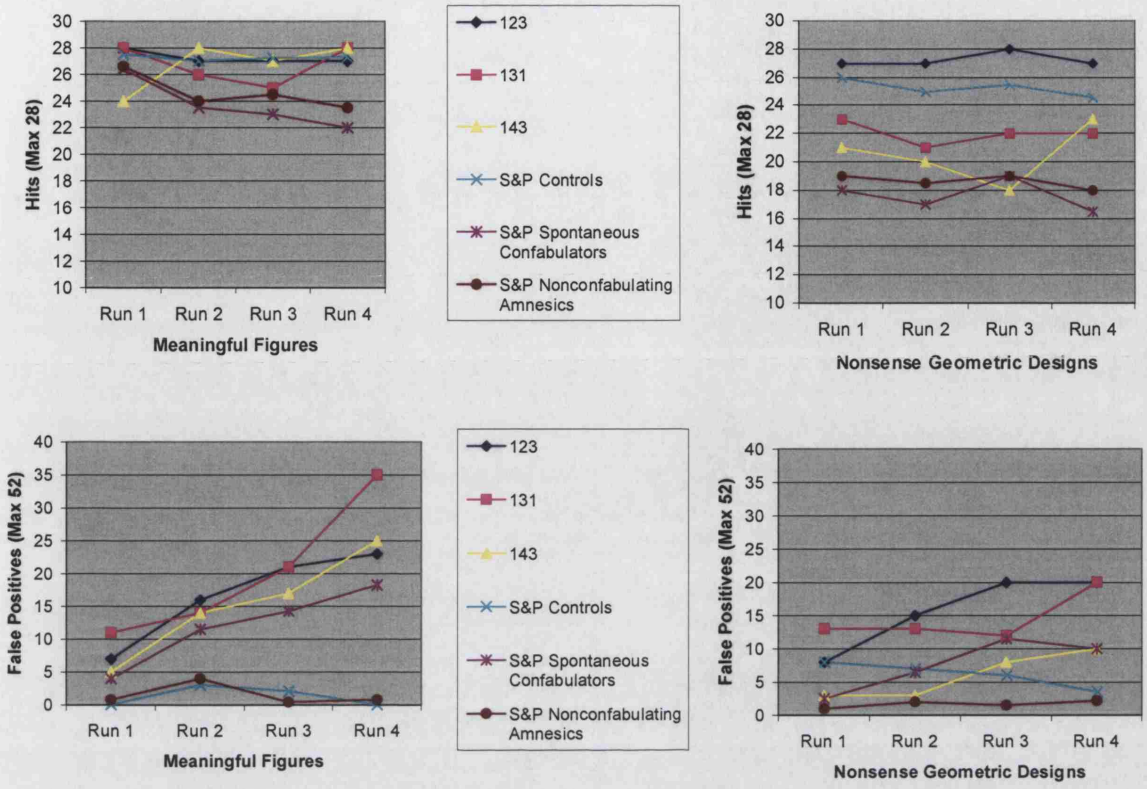

Figure 9.1: Hit Rate and False Positive Performance Across Runs

131 in particular shows a constant false positive rate across the first three runs, which then increases in the fourth) it is still notable that whilst the controls and nonconfabulating amnesics show a stable or decreasing false positive pattern, the spontaneous confabulators, and our three patients all show an increase from run 1 to run 4.

The present data therefore provide support for Schnider and colleagues previous findings. Their task does indeed seem to produce a characteristic pattern of responding in spontaneous confabulators. However some questions remain to be addressed regarding their interpretation of this pattern. Firstly, is there evidence for temporal confusion in these patients that might explain the false positive pattern in these patients? And secondly is there any evidence that past events intrude into the present and that patients then fail to suppress them? Two experimental tests were devised to address these issues.

9.6 RECENCY JUDGEMENT TASK

Design and Procedure:

In order to explore our patients' ability to judge recency we devised a continuous recognition task consisting of 160 presentations of landscape paintings on a computer screen. These presentations were drawn from 40 stimulus paintings, of which 20 occurred twice, and 20 occurred six times within the run. The patients were required to monitor item recurrences throughout the run by indicating to the examiner whether or not they had already seen each image within the run. The task was self-paced, so that a response was gained for each image before the next image was presented. On the final presentation of each item (the second presentation for 20 of the images, and the sixth presentation for the other 20 images), if the patients correctly indicated that they had seen the item before, they were asked to estimate how many items ago they had last seen that image. Within each set of 20 images the penultimate presentation was 5, 10, 20 or 40 items before the test presentation, with each frequency occurring five times. Subjects were asked if they last saw that particular image presented 5, 10, 20 or 40 images ago in the run. The last occasion on which an image appearing six times occurred was matched to the last occasion on which an image appearing twice occurred in terms of their position in the run, to control for changing criterion as the test progressed. If, as Schnider and colleagues have proposed, spontaneous confabulators are unable to prevent previously relevant items from intruding into the present, we might expect our patients to show a tendency to report images as having occurred more recently than they actually did.

Scoring:

Subjects' response data were transformed by giving a score of 0 each time a subject responded that an image had last been seen five items ago, a score of 1 for each response that an item had last been seen 10 items ago, a score of 2 for each response that an image had last been seen 20 items ago, and a score of 3 for each response that an image had last been seen 40 items ago. Therefore perfect performance across all trials would yield a mean score of 0 for items last presented 5 items ago, 1 for images last presented 10 items

ago, 2 for images last presented 20 items ago, and 3 for images last presented 40 items ago.

Results:

Figures 9.2 and 9.3 show the performance of the three patients and of the five age matched controls on this task for items presented twice and for items presented six times within the run.

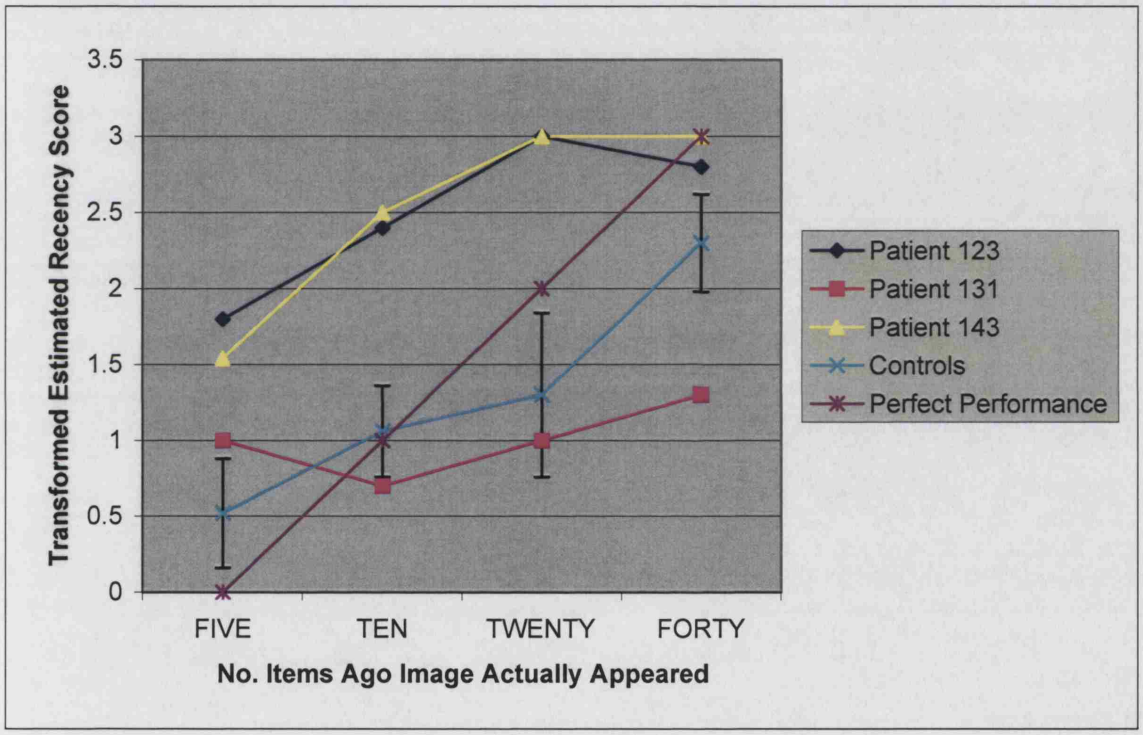

Figure 9.2: Estimated Recency for Items Presented Twice

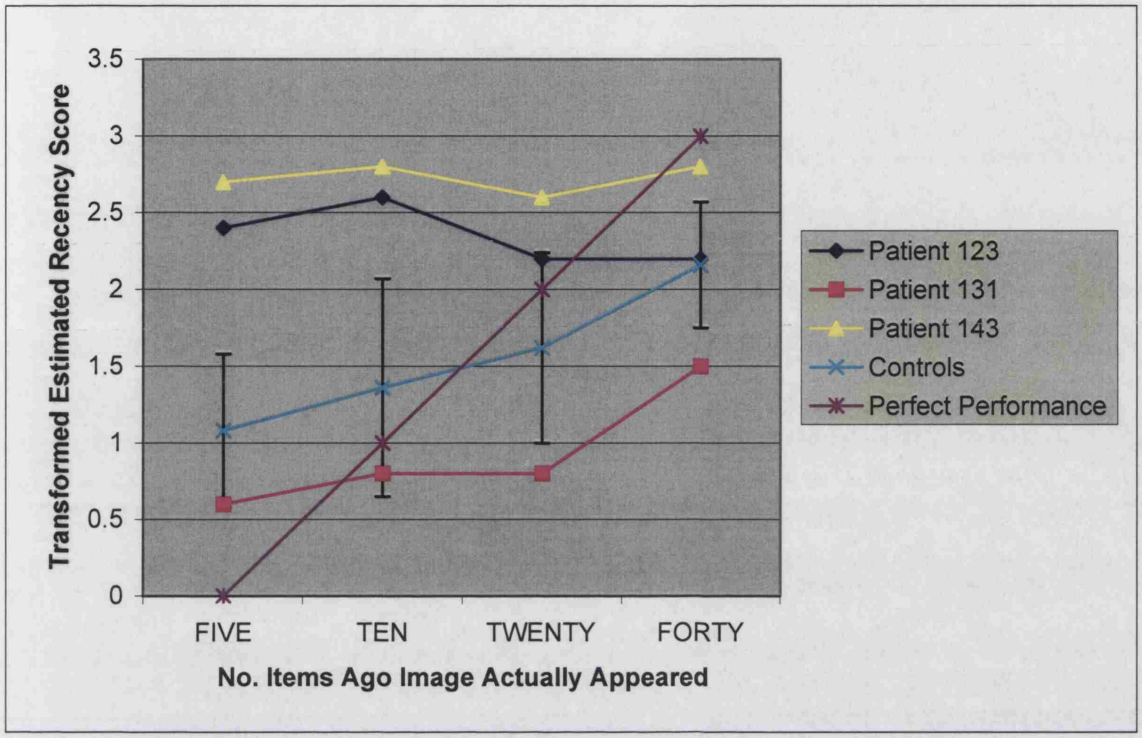

Figure 9.3: Estimated Recency for Items Presented Six Times

Jonckheere trend tests were conducted to investigate whether our subjects' estimates of recency showed an increasing trend as the real time elapsed since presentation increased. For images presented twice within the run, all five control subjects showed a significant trend, with estimates of recency increasing in line with actual time elapsed since presentation. Patient 123 also showed a significant trend (J-T = 21.638, p = 0.008), as did Patient 143 (J-T = 2.879, p = 0.004), but Patient 131 showed no significant trend (J-T = 0.371, p = 0.711). Whilst two of the patients did show some sensitivity in this condition, the control performance was clearly superior.

For items presented six times within the run, four of the five control subjects showed a significant trend, whilst none of our patients showed any effect of increasing time elapsed on their estimates of recency (Patient 123: J-T = -1.022, p = 0.307; Patient 131: J-T = 1.573, p = 0.116; Patient 143: J-T = 0.273, p = 0.785). Examination of figure 9.4 shows that the graphs tend to be flatter in this condition. This is likely to reflect the fact that all

images in this condition have been seen five times before, therefore as well as the most recent presentation whose recency subjects were required to estimate, there are also four earlier memory traces available. Recency might therefore be expected to be overestimated in this condition. Indeed for patients 123 and 143, and for the control subjects, this appears to be the case, with more recently presented items being judged as having occurred longer ago than in the "twice presented" condition. Patient 131 however does not appear to show this effect, possibly in keeping with the fact that even in the "twice presented" condition, his estimates of recency showed no relationship with actual recency at all. The "six times presented" condition evidently increases confusion between memory traces. However although 4 out of 5 of our control patients' estimations still showed some relationship with real elapsed time since presentation, all of our patients estimates ceased to show any relation with real elapsed time. Their ability to judge the recency of presented items is clearly impaired.

To further explore the difference between our patients and controls ability to judge recency we calculated a mean deviation score for each subject, by taking the average of the deviation of their estimates from perfect performance at each recency interval. Deviation scores are shown in Table 9.7.

Table 9.7:
Recency Judgement Task: Mean Deviation Scores

	Appeared Twice	Appeared Six Times
Patient 123	1.1	1.25
Patient 131	1.0	0.76
Patient 143	1.08	1.12
Controls	0.59 (SD = 0.13)	0.81 (SD = 0.22)

We then compared the mean deviation scores of our patients to those of our controls using the modified t-test procedure described by Crawford & Howell (1998). This method is more appropriate for comparing single cases to normative data than z-scores when the normative sample has $N < 50$. For items presented twice, all three patients had significantly larger deviation scores than our controls (Patient 123: $t = 3.504$, $p = 0.025$; Patient 131: $t = 2.822$, $p = 0.048$; Patient 143: $t = 3.368$, $p = 0.028$). For items presented

six times, no significant differences were found between the mean deviation scores of any of our patients and controls, again reflecting the increased difficulty of distinguishing between the greater number of memory traces available for these items in estimating recency.

Finally, we explored whether there was any tendency in our patients to estimate that items had been presented more recently than they actually had. If this were the case then it would support the idea that the critical impairment underlying spontaneous confabulation is the intrusion of previously relevant but now irrelevant memories into the present. However it is immediately apparent from figures 9.3 and 9.4 that two of our patients show exactly the opposite pattern. Both Patient 123 and Patient 143 have a tendency to report items as having last occurred *longer ago* than they actually did. Wilcoxon signed ranks tests confirmed this observation both for items appearing twice (Patient 123: $T = 6$, $p < 0.001$; Patient 143: $T = 9$, $p < 0.001$) and for items appearing six times (Patient 123: $T = 16$, $p < 0.02$); Patient 143: $T = 15$, $p < 0.01$). Patient 131 on the other hand showed no significant tendency either to under or over estimate how recently he had seen the images, either for items presented twice ($T = 9$, $p > 0.05$) or for items presented six times ($T = 15$, $p > 0.05$). This was the same pattern as shown by Controls (all analyses $p > 0.05$). Our patients therefore show no evidence of a fundamental inability to keep currently irrelevant items out of the present.

9.7 TEMPORAL SOURCE IDENTIFICATION TASK

Design and Procedure:

To further explore the temporal memory abilities of our patients we designed a second task examining the ability to discriminate between items presented at two different times. We presented two sequences of 80 images to subjects, separated by a 30 minute delay. Each sequence was made up of 30 different items, 10 of which occurred 6 times within the run, and 20 of which occurred only once. Subjects were asked to indicate item recurrences within the run by pressing the space bar each time they saw an image that

they had already seen. After a 30-minute filled interval the second sequence (with completely new images) was presented with the same instruction to indicate item recurrences. Immediately after presentation of the second sequence subjects completed an unexpected recognition test, consisting of 60 items: 20 from the first sequence (of which ten had been presented 6 times and ten had been presented once), 20 from the second sequence (of which 10 had been presented six times and ten had been presented once), and 20 new distracter items. Subjects were asked to indicate which items they had seen in one of the earlier sequences, and to try to identify which sequence those items had been presented in. Two versions of the task were administered in separate testing sessions – one using meaningful images drawn from Snodgrass & Vanderwart (1980), and one using the nonsense geometric figures designed by Schnider & Ptak (1999).

This test allowed a measure of three aspects of memory functioning in these patients. Firstly it yielded a recognition measure which allowed us to compare the hit rate of our patients against those of controls. Secondly it allowed us to investigate the ability of spontaneous confabulators to identify the source of their memories when the only discriminating information available to them was temporal – whether they had seen the item immediately before the recognition test, or 30 minutes previously. Finally it allowed another test of whether old items intrude into the present. Again we expected that if the patients were unable to prevent old and currently irrelevant memories from intruding into the present, they would show a tendency to misattribute items from sequence one to sequence two in the subsequent recognition test.

Results: Recognition

Performance on the continuous recognition part of the task (during presentation of the sequences) for the three patients and five age-matched controls can be seen in table 9.8.

Table 9.8:
Temporal Source Identification Task: Continuous Recognition Performance

	Patient 123	Patient 131	Patient 143	Controls
SNODGRASS VERSION				
Sequence One Hits / 50	50	49	49	50 (0.00)
Sequence One False Alarms	0	0	1	0 (0.00)
Sequence Two Hits / 50	49	50	45*	49.8 (0.45)
Sequence Two False Alarms	0	3*	2*	0.2 (0.45)
ABSTRACT VERSION				
Sequence One Hits / 50	47	35	45	44.4 (6.35)
Sequence One False Alarms	0	4	6	2.8 (2.59)
Sequence Two Hits / 50	46*	25*	44*	49.2 (0.84)
Sequence Two False Alarms	1	7*	3	2.2 (1.92)

* indicates performance > 2 SD outside the normal range.

The recognition performance in terms of hit rate of the patients is generally preserved and comparable to controls, with the exception of Patient 131 whose performance dropped on the abstract version of the task which was more challenging. There is a tendency toward high false alarm rates in the performance of Patient 131 and Patient 143.

Table 9.9 shows basic performance on the subsequent unexpected recognition test following both continuous recognition sequences

Table 9.9:
Temporal Source Identification Task: Recognition Performance

	Patient 123	Patient 131	Patient 143	Controls
SNODGRASS				
Hits – Items presented once (Max 20)	13	13	20	15.8 (4.02)
Hits – Items presented six times (Max 20)	20	19	20	20 (0.00)
False Alarms (Max 20)	3*	1	3*	0.2 (0.45)
ABSTRACT				
Hits – Items presented once (Max 20)	4	6	10	11.8 (4.60)
Hits – Items presented six times (Max 20)	15*	14*	14*	18.8 (1.79)
False Alarms (Max 20)	3	4	5	4 (2.45)

* indicates performance > 2 SD outside the normal range

Again the recognition performance of the patients is preserved in the easier Snodgrass version of the task, with a slightly elevated false alarm rate. In the more difficult Abstract version of the task the hit rate amongst the patients falls somewhat but the false alarm rate is within normal limits.

Results: Temporal Source Discrimination

In the following analyses of sequence discrimination, data are collapsed across both the Snodgrass and Abstract versions of the task. Figures 9.4 and 9.5 show the mean accuracy of patients and controls in attributing recognized items to sequence one or two, for items that were initially presented only once, and for items that were presented six times. As this is a 2-alternative forced choice task, the chance performance level is 50%.

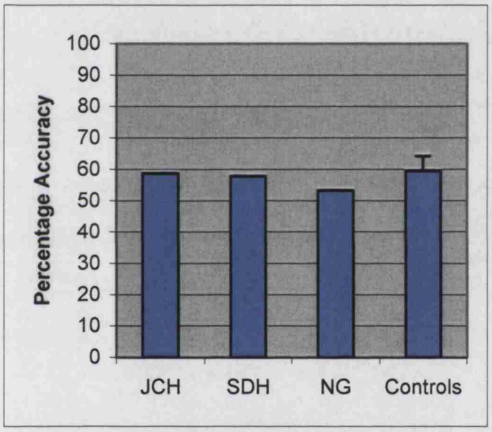

Figure 9.4: Items presented once.

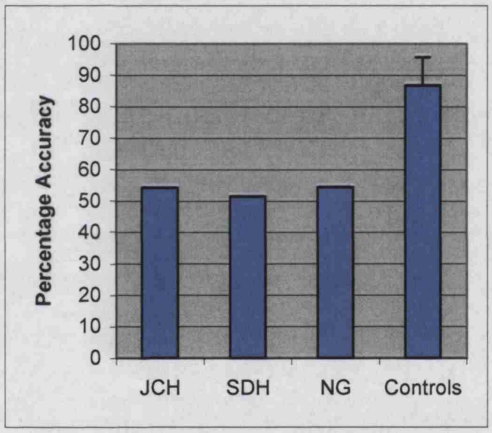

Figure 9.5: Items presented 6 times.

When to-be-remembered items have only been presented once within a sequence, both the patients and controls are poor at correctly identifying whether they were initially seen within the first or second sequence. However when items have been presented six times within a particular sequence, creating a stronger memory trace, normal controls are able to correctly identify their source on 86.6% of occasions. However the confabulating patients, whilst able to recognize previously encountered items at a rate approaching that of controls, remain completely unable to identify the source of their familiarity. They are completely at chance in identifying whether they saw the item immediately before the recognition test, or 30 minutes previously.

Binomial analysis of the results for items presented six times confirms this, with no patient differing significantly from chance in the proportion of items assigned to the correct source (Patient 123: 19/35 correct, $p = 0.37$; Patient 131: 17 / 33 items correct, $p = 0.5$; Patient 143: 18 / 33 items correct, $p = 0.36$). In contrast all five control subjects showed a highly significant difference, with the majority of recognized items being assigned to the correct source, (all results $p < 0.02$). Modified t-tests also reveal that each patient differs significantly from the control group in their percentage accuracy in identifying the source of items presented six times (Patient 123: $t = -3.32$, $p = 0.03$; Patient 131: $t = -3.60$, $p = 0.02$; Patient 143: $t=-3.30$, $p = 0.03$).

Results: Intrusions of Old Items into the Present

Again, analysis of the type of errors made by the confabulating patients in assigning their memories to one of the two sequences is revealing. If they suffer an inability to prevent previous memories from intruding into the present one might expect them to show a tendency to incorrectly assign items that they had seen in the first sequence to the second, just presented, sequence. Table 9.10 shows the number of items incorrectly attributed to sequence 1 (Moved to the past) and incorrectly attributed to sequence 2 (Intruding into the present) by each of the three confabulating patients.

Table 9.10:
Temporal misattribution of items by confabulating patients

	Moved to the past	Intruding into the present
Patient 123	15	8
Patient 131	12	12
Patient 143	23	6

Binomial analysis for Patient 123 reveals no significant trend to assign more memories incorrectly to sequence 2 than sequence 1 (8 versus 15, $p = 0.11$). Indeed he shows a non-significant trend in the other direction. Similarly Patient 131 shows no tendency to misattribute items to sequence 2 rather than sequence one (12 vs 12, $p = 0.58$). Patient 143 does show a significant bias in his attribution of recognized items to a particular sequence (23 vs 6, $p = 0.001$). However this is in the opposite direction to that which

might be predicted by Schnider and colleagues' theory. Patient 143 has a significant tendency to say that items were encountered in the first sequence rather than the second, current one. Again our data shows no support for an inability to keep remembered items out of the present. It simply shows a complete inability to place recognized material in its correct temporal context.

9.8 INTERIM SUMMARY

Investigations with our three confabulating patients have provided support for Schnider and Ptak's (1999) reports of a characteristic pattern of performance on their continuous recognition task. Like their spontaneously confabulating group, our patients showed a constant hit rate across runs in combination with a steep increase in false positive responses. However our results do not provide support for the cognitive mechanism proposed by Schnider and colleagues to underly this pattern of performance. We found no evidence of an inability to keep memory traces out of the present. Instead we found that our spontaneously confabulating patients simply have a complete inability to place remembered information in its correct temporal context.

It is tempting to conclude that this in itself is sufficient to guarantee failure on the Schnider & Ptak (1999) continuous recognition task. However one of the most striking aspects of Schnider and colleagues' work is their assertion that their task can distinguish between confabulating and non-confabulating amnesics, whilst traditional temporal tasks are failed by both groups. There are potential problems associated with this explanation, which are raised in the discussion, and which indicate that temporal confusion may after all be sufficient to account for the pattern of performance shown by these patients. However, even if this is the case, it seems obvious that temporal confusion can only be a partial explanation for confabulation. Temporal confusion explanations of confabulation cannot explain single content-specific confabulations such as that reported by Burgess & McNeil (1999), as general temporal confusion would be expected to have a general effect. Neither can they explain bizarre and fantastic confabulations such as those produced by patient 143. Even though a confusion of temporal source or current

relevance may play some part, it cannot explain how such bizarre ideas arise in the first place, and are accepted as reality. One clue to a further mechanism that may contribute to the production of confabulatory ideas comes from examination of our patients' performance on the reality monitoring task.

9.9 REALITY MONITORING TASK

One of the tests that formed part of our general battery for frontal patients may suggest another dimension to the mechanisms involved in spontaneous confabulation. The reality monitoring task (described in chapter 6) assessed the ability to distinguish between real and imagined events by asking patients to identify the source of words that were new, previously heard, or previously imagined. Previous theorising about the relationship between confabulation and reality monitoring (Johnson, 1997) would predict that confabulating patients should show a tendency to misattribute imagined events to real occurrences.

Results:

The performance of the three confabulating patients, along with the performance of the battery control group and the battery frontal group (with the three confabulating patients excluded) is shown in figure 9.6.

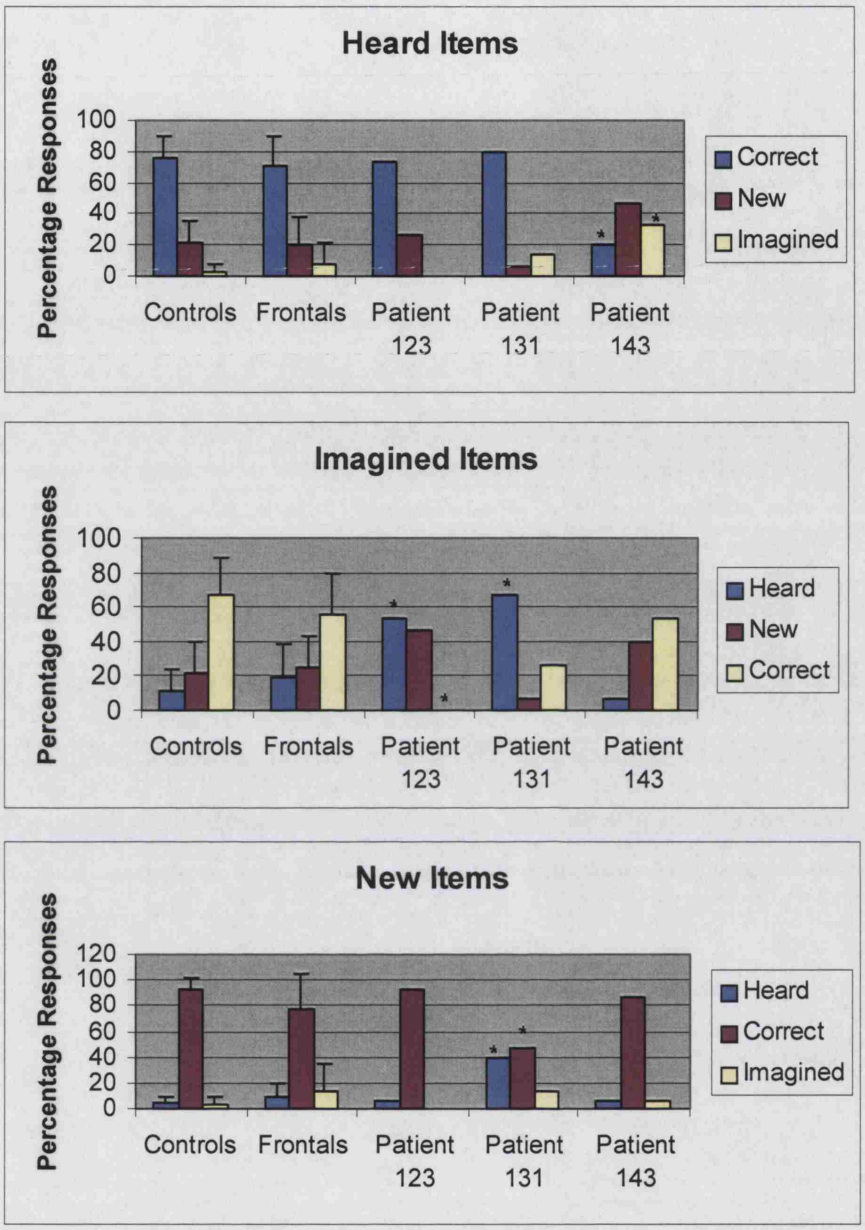

Figure 9.6: Initial Performance in Reality Monitoring Task

(* = significantly different from controls at p = 0.05)

Examination of the data suggested that there might be a characteristic difference in the way that the confabulating patients and the controls responded in this task. In particular, Patient 123 and Patient 131 seemed to have a strong tendency to identify words that they had imagined as words that had been read to them. Indeed Patient 123 failed to identify any of the words he imagined correctly.

The patient data was compared to control performance with the modified t-test procedure described previously, and significant differences at the $p = 0.05$ level are indicated with an asterisk in figure 9.7. Patient 123 correctly identified significantly fewer of the imagined words than controls, and attributed a significantly higher number of them to the heard category. Similarly, Patient 131 attributed significantly more of his imagined words to the heard category than controls. He was also significantly less likely to correctly identify the new, distracter items, tending to identify them as heard items. Patient 143 showed a rather different pattern of performance, identifying significantly fewer of the heard words than the controls, tending to identify them as imagined.

To confirm that the confabulating patients understood the task, and were able to use the "imagined" category correctly as a response, a simplified version of the task was administered. In this task two stimulus items were presented, one word read aloud and one prompt to imagine. Immediately following this they were given a three item forced choice recognition test, in which one word was the read word, one was the imagined word, and the other was a new distracter word. They were asked to identify which of the words they had just heard, which they had just imagined, and which was new. The same task was carried out with fifteen pairs of stimuli, immediately followed by the three-choice recognition test. This task therefore differed from the experimental task only in terms of memory load, allowing us to confirm the patients ability to identify the source of words they have just encountered. The results of this simplified task can be seen in figure 9.7.

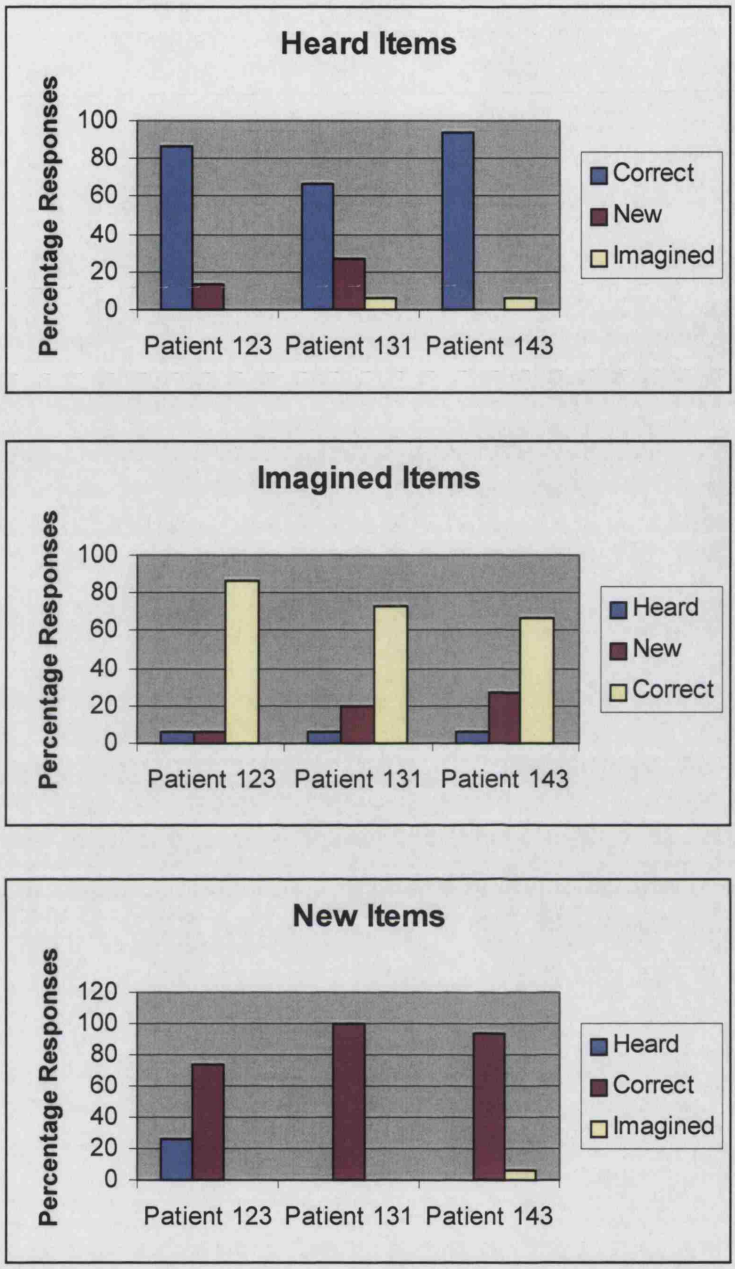

Figure 9.7: Performance on the Simplified Reality Monitoring Task

It is immediately apparent that although performance is not perfect on this task, all three patients are capable of correctly identifying the source of their memories when memory load is reduced. None of the patients have an inability to correctly use any of the response categories. Immediately after administration of the simple reality monitoring task, the

original version was repeated in an attempt to replicate our results. The results from this second administration can be seen in Figure 9.8.

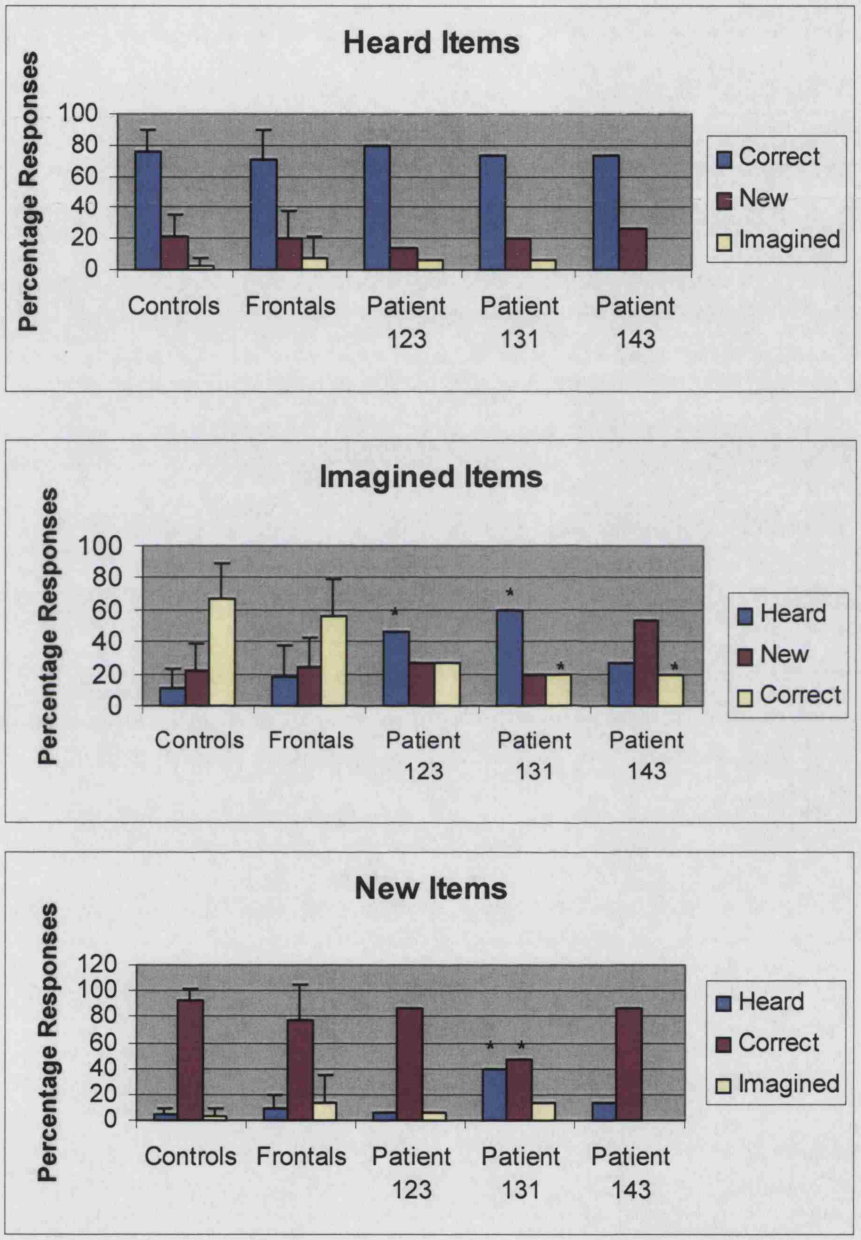

Figure 9.8: Repeat Performance on Reality Monitoring Task

(* = significant at p = 0.05)

On second administration Patient 123 is now more able to identify occasional imagined items (4/15), but still has a significant tendency to think that they were read to him by the

examiner. Patient 131 too continues to misidentify imagined items as heard, and to misidentify new words as heard. Patient 143 shows the biggest change in his pattern of responding from the first to second administration, and is now identifying significantly fewer of the imagined words than controls.

Signal detection theory was used to explore the patients' sensitivity to the task on each administration compared to controls. For this analysis the "Heard" and "Imagined" categories were collapsed and compared to "New" items. Data are presented in table 9.11.

Table 9.11:
Reality Monitoring Task: Signal Detection Data

	Patient 123 1st Admin	Patient 123 2nd Admin	Patient 131 1st Admin	Patient 131 2nd Admin	Patient 143 1st Admin	Patient 143 2nd Admin	Controls
d'	1.84	1.95	1.41	0.76*	1.28	1.36	2.31 (0.57)
β	2.91	1.30	0.33	0.70	1.83	1.80	2.45 (1.35)

The only significant difference between the patients and controls was a drop in Patient 131's sensitivity on the second administration of the task, which means that caution is required in drawing conclusions from his pattern of responding.

Taken together the results from the reality monitoring task may offer a clue to an additional possible mechanism at work in spontaneous confabulation. Confabulating patients, despite showing normal recognition performance, seem to have difficulty identifying the nature of an experience compared to controls. In two of our patients, this difficulty is manifest as a significant tendency to misidentify imagined events as real.

9.10 DISCUSSION

Single case investigations with three spontaneously confabulating patients have provided further replication of the pattern of performance reported by Schnider and colleagues on their continuous recognition task. Spontaneous confabulators do seem to show a

characteristic pattern of performance in which a constant hit rate is accompanied by a steeply increasing false positive rate run to run. The results reported in chapter 8 indicate that this pattern of responding is not shown by frontal patients in general, and that this task may reliably distinguish between confabulating and non-confabulating patients. However the explanation offered by Schnider and colleagues for their results was not supported by our findings. Schnider and colleagues argue that the fundamental deficit in spontaneous confabulation is "a failure to suppress evoked memories that do not pertain to ongoing reality". Thus "associations of old, firmly established information would intrude into ongoing thinking" (Schnider, 2001, p 154). However in two experiments reported here we found no evidence that previously encountered events are experienced as having occurred more recently than they actually did. In fact if anything there was a trend in two out of three of our patients to think that events had occurred longer ago. There was also no evidence that our patients produced large numbers of previous-item intrusions in the verbal and visual organisation and monitoring tasks, which would have indicated an intrusion of inappropriate old associations into the present (see also Moscovitch & Melo, 1997). What was evident from the results of these two experiments was the extent of the temporal confusion in these patients. Our three patients were completely unable to make temporal discriminations either in terms of recency judgements, or in discrimination of two temporal sources. It could be argued that this temporal confusion is sufficient in itself to guarantee failure on the Schnider & Ptak task.

The problem with positing temporal confusion as the cause of failure on this task is that it is claimed not to consistently distinguish between confabulating and non-confabulating patients. Schnider & Ptak (1999) claim that their task can distinguish between confabulating and non-confabulating amnesics, whilst the previous literature indicates that traditional temporal tasks are failed by both groups. The current study of course used a frontal rather than an amnesic series, but appeared to show the same pattern. The findings presented in Chapter 8 indicated that the continuous recognition task may distinguish between confabulating and non-confabulating frontal patients. In contrast there is substantial previous evidence that frontal patients in general have difficulty with traditional temporal tasks (e.g. Butters et al, 1994; Daum & Mayes, 2000; Kesner et al,

1995; McAndrews & Milner, 1995; Shimamura et al, 1990; Smith & Milner, 1988; Stanhope et al, 1998). Schnider and colleagues argue instead that their task involves some other function that does not require conscious temporal discrimination processes: "...no distinction of the recency of last appearance nor knowledge about the temporal relationship among pieces of information is required" (Schnider 2001, p 153). Similarly; "our task does not demand distinction between information sources or contexts in the past, rather it demands the ability to refer a memory evoked by the repeated presentation of an item to its own previous occurrence - either in the current run, the "now", or a previous run" (Treyer et al, 2003, p 611). And Schnider et al (2002) state again that the suppression process that underlies performance on their task operates via "an online filtering mechanism matching currently active memory traces with currently available external information, rather than on construction of a reality representation based on the recency of activated memory traces" (p 59).

However it is unclear then exactly how their task *is* successfully carried out. It seems intuitive that it must rely on some sort of temporal discrimination, either in judging the recency of presentation of a particular item, or in associating it with its correct temporal context (previous or current run). Indeed this is what subjects report they are doing whilst carrying out the task. Further research is required to investigate whether traditional temporal tasks might also distinguish between confabulating and non-confabulating patients. Although Schnider & colleagues claim that other temporal tasks have not been shown to specifically affect confabulating patients this has actually not been explicitly investigated. Most reports give no details about the presence or absence of confabulation (Butters et al, 1994; Daum & Mayes, 2000; Kesner et al, 1995; Kopelman et al, 1997b; Milner et al, 1985, 1991; Shimamura et al, 1990; Stanhope et al, 1998). One study has compared a confabulating patient to 3 non-confabulating frontal patients (Johnson et al, 1997). They reported that their confabulating patient was not impaired on a list discrimination task, whereas the non-confabulating patients were. This is an intriguing result, as the three confabulating patients presented here clearly do have impairments of temporal memory. However further studies investigating this issue are required. It may be

that other temporal tasks are in fact able to distinguish between confabulating and non-confabulating frontal groups.

Previous studies of temporal memory have used a variety of temporal tasks that may be less demanding than the Schnider & Ptak (1999) task in their temporal discrimination requirements. In this task the repeated use of targets creates considerable confusion. It is likely that it demands rather different processes than frequency estimation, for example. The temporal discrimination tasks described in this chapter would appear to involve fewer processes than the Schnider & Ptak task, yet the three confabulators were completely at chance on them. It is necessary to explicitly establish whether non-confabulating patients with extreme temporal confusion do actually show preserved performance on the Schnider task. Again, this has not been investigated. Further research is required therefore to investigate whether some sort of temporal discrimination may be a sufficient explanation for failure on the Schnider & Ptak (1999) task. However, if it is not, then the Schnider & Ptak task does indeed seem uniquely able to tap the critical impairment underlying confabulation. In this case, clearer specification of how the task is carried out in the absence of temporal discrimination is required. Certainly on the basis of our results there is no evidence that it involves suppression of currently irrelevant memory traces.

One other difficulty with the Schnider account is the assertion that in the healthy brain, associations that do not pertain to current reality are suppressed or deactivated even before they reach consciousness. This is based on an ERP study in which correct suppression of distractors was associated with alteration of cortical activity after 220-300 ms, compared to learning and recognition which was characterised by cortical amplitude modulation after 400-480 ms. This early activity is interpreted as suppression of a processing stage rather than an additional cortical process, and is presumed to be the cortical expression of an anterior limbic suppression mechanism that actually occurs even earlier (Schnider *et al*, 2002). Thus "before the content of an evoked memory is recognised, it has already been checked and adjusted according to whether it relates to ongoing reality or not" (Schnider, 2001, p 158). Schnider *et al* (2002) argued that the fact

that the suppression process is preconscious may offer an explanation for the absolute conviction these patients exhibit that their imagined reality is true. However it seems implausible that this process does not occur consciously, after a stimulus has been recognised, as is dependent on task instructions. For example, having a preconscious filtering mechanism which excluded items not pertaining to now would be a distinct disadvantage if the task instructions were reversed and participants had to respond only to items encountered in the previous run, not in the current run. In order to function in a day-to-day sense it is critical that we have all relevant information consciously available to us, and that any monitoring or choosing between stimuli is done consciously on the basis of current demands. There is though the possibility that the early activation reported by Schnider *et al* (2003) in association with correct rejection of currently irrelevant items might reflect some kind of temporal tagging of information as "past", which can be later used for monitoring according to the task requirements, rather than a preconscious suppression of currently irrelevant traces.

The other problem facing any "Temporal Context Confusion" account of confabulation is that not all confabulations are easily explicable in terms of a temporal misplacement of true events. One clue to an additional process that might be involved is the performance of the confabulating patients on the reality monitoring task. The evidence presented here suggests that confabulating patients may have difficulty in identifying the nature of an experience, and that in some cases (2 out of 3 of our patients) this may take the form of a bias to misidentify imagined events as real. If the confusions suffered by confabulators not only encompasses mixing up events in time, but also mixing up reality and imaginings, then confabulations such as those produced by patient 143 are more explicable. However reality monitoring failures are also unable to provide a full explanation of confabulation. Reality monitoring failure has been reported in both confabulating and non-confabulating patients (Johnson *et al*, 1997), and even where difficulties are reported they do not always take the form of a bias to misidentify imagined events as real (patient 143 this chapter; patient GA, Dalla Barba *et al*, 1997). It is likely that spontaneous confabulation involves a combination of difficulties, including deficits in the availability of, or monitoring of, all types of source information; temporal,

spatial, and internal/external, in combination with a breakdown in plausibility judgements that allow fantastic ideas to be accepted as real. This argument is developed further in the general discussion.

Neuroanatomy:

Schnider and colleagues also claim that their task has anatomical specificity, and that it selectively involves the anterior limbic system. Specifically in clinical studies they have identified the basal forebrain, amygdala and perirhinal cortex, the dorsomedial thalamus or its connections with the OFC in the capsular genu, or the medial hypothalamus and the medial orbitofrontal cortex. A more recent PET study revealed consistent activation in the left caudate nucleus (ventral striatum, head and body of the caudate), the left substantia nigra and ventral tegmental area, and the right medial thalamus (Treyer *et al*, 2003).

Regions identified in the confabulation literature in general have also been largely consistent with the work of Schnider and colleagues. Damage following ruptured aneurysms of the ACoA, which frequently lead to confabulatory disorders, tends to be restricted to the posterior aspect of the ventromedial frontal lobe, encompassing the orbitofrontal cortex and midline and paramedial basal forebrain. Confabulation has most often been attributed to damage to these regions in association with additional frontal damage (DeLuca, 1993; DeLuca & Cicerone, 1991; DeLuca & Diamond, 1995; Fischer *et al*, 1995; Vilkki, 1985). It has also been reported in association with basal forebrain damage alone, in the absence of frontal pathology. Morris *et al* (1992) and Hashimoto *et al* (2000) for example highlighted the septal nuclei and diagonal band of Broca as critical lesion sites. However these regions are involved in limbic circuits involving the orbitofrontal cortex, indicating that even in the absence of overt frontal damage, the orbitofrontal cortex may still be critical.

Analysis of the lesion sites in the three confabulating patients reported here is limited due to scan quality. However all three of them had lesions affecting the orbitofrontal cortex. Patients 123 and 143 were included in the "Orbital" grouping for level 2 analysis, as this

represented the area of greatest damage. Patient 131 was not included in level 2 groupings as his lesion was too extensive to be classified into just one area, but involved extensive orbitofrontal damage. More specifically they were coded on the lesion protocol as having damage in the following areas:

Patient 123: Left orbital only.
Patient 131: Right and left orbital, right and left sub genu, right and left anterior cingulate, left superior frontal gyrus on both the medial and lateral surfaces.
Patient 143: Left and right orbital.

The common areas centred on the left orbital surface, more medial than lateral, and more posterior than anterior. These lesion areas are consistent with a key role for the posterior medial orbitofrontal cortex in spontaneous confabulation.

CHAPTER TEN:
GENERAL DISCUSSION

The frontal lobes are clearly not homogeneous anatomical or functional structures. However previous research has been limited in its capacity to elucidate the functional specialization of specific subregions of the frontal lobes in memory. The results reported in this thesis begin to offer some clues as to the memory control processes overseen by the frontal lobes, and the specific areas with which they are associated. Although these results require replication, the methodology employed here has already allowed some direct comparisons to be made with findings from neuroimaging. In this chapter a summary of the memory impairments which are associated with damage to the frontal lobes, and specifically to the Left Lateral, Right Lateral, Orbital and Medial subregions of the frontal lobes is presented. These findings are discussed in terms of previous neuropsychological and neuroimaging findings. Then the findings relating to confabulation are summarised, and discussed in terms of the theories of confabulation and autobiographical memory presented in Chapter 1.

10.1 Which Memory Impairments Follow Frontal Lobe Damage?

Investigation of the memory impairments in this clinical series revealed general frontal impairments in both recognition memory (in the RMT and Doors and People Task, Chapter 3, and the Continuous Recognition Task, Chapter 8), and in recall memory (in Story Recall, The Rey Complex Figure Test and The Doors and People Task, Chapter 3, The Verbal and Visual Organisation and Monitoring Tasks, Chapter 5, and the Encoding Specificity Task, Chapter 6). Some previous authors have suggested that patients with frontal lobe lesions have a recall impairment with normal recognition abilities, reflecting the greater strategic demands present in recall tasks (Hanley *et al*, 1994; Janowsky *et al*, 1989, Jetter *et al*, 1986; Milner *et al*, 1991, Shimamura *et al*, 1991; Stuss & Benson 1984). However the present results indicate a more severe memory impairment in this sample, extending to recognition abilities as well. Impaired recognition has actually been reported several times in frontal samples (Daum & Mayes, 2000; Delbecq-Derouesne *et al*, 1990; Dimitrov *et al*, 1999; Kopelman & Stanhope, 1998; Mayes & Daum, 1997;

Schnyer *et al*, 2004; Stuss *et al*, 1994; Wheeler *et al*, 1995). It appears that recognition impairments may actually be a feature of frontal lobe damage, and previous studies may have failed to find effects either because of low power due to small sample sizes (Wheeler *et al*, 1995) or because of ceiling effects (Kopelman & Stanhope, 1998). The finding that both recall and recognition abilities are impaired in our sample is consistent with neuroimaging studies that have reported similar activation of the frontal lobes in both recognition and recall tasks (Cabeza *et al*, 1997a).

More specific investigation of whether the recall deficit in the sample may be due to impairments at encoding or retrieval revealed mixed results. In the verbal and visual OM tasks (Chapter 5) there was no effect of organisation at encoding (i.e. whether the words or images were presented blocked or were presented randomly). This implied that there was no strategy deficit at encoding in the sample. There was also no general Frontal effect of prompting with category cues at recall, implying that there was no strategy deficit at retrieval. These results were surprising in the light of previous suggestions that the recall impairments in Frontal patients are secondary to deficits in strategic organisation at encoding and / or retrieval (Diamond *et al*, 1997; Eslinger & Grattan, 1994; Gershberg & Shimamura, 1991, 1995; Hanley *et al*, 1994; Hirst & Volpe, 1988; Incisa della Rochetta, 1986; Incisa della Rochetta & Milner, 1993; Kopelman & Stanhope, 1998; Stuss *et al*, 1994; Vilkki *et al*, 1998).

However in the Encoding Specificity Task (Chapter 6) the Frontal group made significantly fewer correct choices at encoding than the Control group. Although this is not a direct measure of encoding, it does indicate a reduced ability to use semantic information appropriately, which is known to impact upon the depth of encoding operations and subsequent recall (Craik 2002; Craik & Lockhart, 1972). Examination of the recall data in this task revealed that the Frontal group had impaired recall both when raw recall rates were examined, and when recall was examined only for those items correctly encoded. This indicates that recall deficits in the frontal group were likely to be a result of impairments at both encoding and at retrieval. This is one example of where analysis of the Frontal group as a whole concealed differential effects that were actually

present in specific Frontal subgroups. These findings relating to deficits at encoding versus deficits at retrieval are discussed further below.

Intrusions and false recognition are frequently reported in association with frontal lobe damage (Alexander *et al*, 2003; Baldo *et al*, 2002; Budson *et al*, 2002; Daum & Mayes, 2000; Delbecq-Derouesne *et al*, 1990; Curran *et al*, 1997; Mayes & Daum, 2997; Melo *et al*, 1999; Parkin *et al*, 1996, 1999; Rapcsak *et al*, 1994, 1996, 1999; 2001; Schacter *et al*, 1996; Swick & Knight, 1999; Verfaillie *et al*, 2004; Ward & Parkin, 2000; Ward *et al*, 1999). However we found no increase in false recognition in our frontal group in either the famous faces task (Chapter 3) or in the continuous recognition task (Chapter 8), and no increase in intrusions in either the Story Recall task (Chapter 3) or in free recall in the verbal OM task (Chapter 5). This was more consistent with Alexander *et al* (2003), Dimitrov *et al*, 1999, Incisa della Rochetta (1986), Jetter *et al* (1986) and Stuss *et al* (1994), who did not find significantly higher rates of intrusions in their frontal groups compared to controls.

However a tendency towards false positive responding in the Frontal group was revealed in the Reality Monitoring task (Chapter 7), and we did find increased rates of intrusions in the Frontal group in the Visual OM task (Chapter 5), increased rates of new word intrusions in the Encoding Specificity Task (Chapter 6) and increased rates of extra list intrusions after prompting in the Verbal OM Task (Chapter 5). The fact that intrusion effects were found in some tasks and not others is likely to be due to differential sensitivity between tasks, and the large variances in some groups. However it seems that at least under some circumstances false recognition and intrusions in recall may be a feature of frontal lobe damage (and more interesting regionally specific effects are discussed below). The fact that the intrusions in the Encoding Specificity Task and the Verbal OM Task tended to be new items, rather than previously presented items which were recalled in the wrong temporal context, was surprising in the light of suggestions that patients with frontal lesions have difficulty with temporal memory judgements (Butters *et al*, 1994; Daum & Mayes, 2000; Johnson *et al*, 1997; Kesner *et al*, 1995; Kopelman *et al*, 1997b; Milner *et al*, 1985, 1991; Schacter, 1987; Shimamura *et al*, 1990;

Stanhope *et al*, 1998), and that confabulation may been attributed at least in part to the recollection of true memories in the wrong temporal context (Ptak *et al*, 2001; Ptak & Schnider, 1999; Schnider, 2001; Schnider *et al*, 1996a,b, 2000a,b, 2002; Schnider & Ptak, 1999; Treyer *et al*, 2003). The intrusions elicited in these paradigms were new words which had not been previously encountered, although they may have been semantically related to the encountered words.

A more extreme example of intrusion of incorrect information was found in the Confabulation Battery (Chapter 4), in which the frontal group produced more confabulations than the Control group in response to questions probing both personal episodic memory and orientation in time. The presence of confabulation was thus confirmed in the sample, and more interesting regionally specific effects are discussed below.

10.1.1 Which Memory Impairments Follow Left Lateral Frontal Lobe Damage?

In Level 2 and Level 3 analyses, in which the performance of the Left Lateral group could be specifically examined, we found no specific deficits in the Verbal or Visual OM Tasks (Chapter 5), the Reality Monitoring Task (Chapter 7), or the Continuous Recognition Task (Chapter 9). The lack of effects on the Verbal OM Task was particularly surprising in the light of previous reports that patients with damage to the left frontal lobe have particularly marked deficits on verbal recall tasks (e.g. Alexander *et al*, 2003; Dimitrov *et al*, 1999; Incisa della Rochetta & Milner, 1993; Stuss *et al*, 1994, Vilkki *et al*, 1998). However in two of these cases (Alexander *et al*, 2003; Stuss *et al*, 1994) left lateral recall impairments were attributed to mild language impairments. Our Left Lateral group did not have any language impairment (as measured by the Graded Naming Test, Chapter 3) so this may be one explanation for the lack of effects found.

However the Encoding Specificity Task (Chapter 6) did reveal some specific Left Lateral subgroup effects. The Left Lateral group in this task had reduced recall rates when raw recall was examined, but this recall impairment disappeared when recall rates were examined only for those items which had been correctly encoded. This indicated a role

for the Left Lateral PFC (amongst other areas) in encoding processes. Planned comparisons in this task showed that in raw recall the Left Lateral group had significantly lower recall rates than the Controls in both the Specific Dimension and the Similar condition. However when corrected recall was examined they differed from Controls only in the Similar condition. This seems to provide some support for Thompson-Schill *et al*'s hypothesis that the left inferior frontal gyrus may be specifically responsible for selecting amongst competing semantic information at encoding, in that it appears that the Left Lateral group's recall impairment in the Specific Dimension condition was due to difficulties at encoding. However planned comparisons failed to reveal any Left Lateral encoding deficit in either condition which would be predicted by their theory. Moreover, specific examination of only those patients with damage to the left IFG revealed no significant results (see also section 10.1.3 below).

In terms of intrusions and confabulations, the Left Lateral group did not produce significantly higher rates of false recognition or intrusions than the Controls in any task. However they did produce more confabulations in response to questions probing personal episodic memory in the Confabulation Battery than controls (Chapter 4). This result was made more interesting by the fact that there was some evidence for a double dissociation between the Left Lateral group and the Right Lateral group on this task. The Left Lateral group produced fewer correct responses and more confabulations in response to personal episodic memory questions, whilst those with damage to the Right Lateral region were more preserved on these measures in the level 3 analyses. In contrast the Right Lateral group produced fewer correct responses and more confabulations in response to orientation to time questions, whilst those with damage to the Left Lateral region were more preserved on these measures in the level 3 analyses. This Left Lateral effect has not previously been reported, and confabulation has been generally associated either with ventromedial or with right lateral rather than left lateral frontal lobe damage. This is the first time that the Confabulation Battery has been used with a general frontal sample, and it will be interesting to see if this left lateral effect, and more specifically this double dissociation, can be replicated in future studies. However it should be noted that the double dissociation reported here does not come from direct comparisons of the Right

and Left Lateral groups, but from a combination of Level 2 and Level 3 analyses. This result should therefore be treated with caution until replication occurs.

10.1.2 Which Memory Impairments Follow Right Lateral Frontal Lobe Damage?

Examination of the Right Lateral subgroup revealed several memory impairments. This group had a reduced hit rate on the Continuous Recognition Task (Chapter 8), and had a specific Verbal Forgetting Impairment on the Doors and People Task (Chapter 3). On both the Verbal and Visual OM Tasks (Chapter 5) they had significantly impaired overall recall rates compared to Controls. This group was specifically affected by the provision of category prompts at retrieval on the Verbal OM task. Following prompting they produced significantly more additional correct recalls than Controls, so were significantly aided by this retrieval manipulation. Prompting also raised their rates of prior list intrusions, but not their rates of extra list intrusions (in contrast to the Frontal group as a whole, who had elevated extra-list intrusions following prompting). This pattern of results strongly indicates that the primary deficit in the Right Lateral group is a strategic or executive deficit at retrieval, which may be overcome by the provision of cues. This external cueing appears to enable this group to adopt a controlled responding strategy which raises their veridical recall without raising the rates of intrusions of non-presented items. However it does raise the rates of prior list intrusions which are more difficult to control for (as they have actually been previously encountered). This argument is supported by the finding in the Encoding Specificity Task (Chapter 6) that in level 3 analysis those patients with Right Lateral damage produced fewer new intrusions than those patients without Right Lateral damage. This group do not adopt an uncontrolled responding strategy whereby semantic associates of the target words are intruded into recall. There is therefore strong evidence that the Right Lateral group suffer from an impairment in their retrieval processes, either in producing cues to start or guide their recall, or in retrieval "effort". However the Encoding Specificity Task also provided evidence that they may have an additional encoding deficit, as the Right Lateral deficit in raw recall was no longer there when recall was corrected for encoding.

In terms of intrusions and confabulation, the Right Lateral group was preserved on a number of measures. In the Reality Monitoring Task (Chapter 7) level 3 analyses revealed that those patients with Right Lateral damage made less "Heard said Imagined" and less "New said Imagined" errors than those without Right Lateral damage, indicating that they were less susceptible to producing "imagined" as a false response. In the Confabulation Battery (Chapter 4) level 3 analysis revealed that those patients with Right Lateral damage produced significantly fewer confabulations overall than those patients without Right Frontal damage. More specifically they also produced fewer confabulations to questions probing personal episodic memory. These results were surprising in the light of some suggestions about the localisation of processes which when impaired produce false recognition, intrusions and confabulation. In addition to the view that it is associated with the basal forebrain, there have been some suggestions that it may also involve right frontal damage (Burgess *et al*, 1996; Delbecq-Derouesne *et al*, 1990; Curran *et al*, 1997; Moscovitch, 1995; Parkin *et al*, 1993; Schacter *et al*, 1996). However the results presented here and in section 10.1.4 and 10.1.5 indicate that the distinction between right lateral and right ventromedial damage is critical in this regard. The one confabulation measure on which patients with Right Lateral damage were impaired was in confabulations to questions probing orientation in time in the Confabulation Battery. This is the measure which produced the double dissociation between Right and Left Lateral damage mentioned previously, and requires further investigation.

10.1.3 Integration of Lateral Frontal Lobe Findings with Evidence from Neuroimaging.

Neither the recall nor the recognition measures employed in this battery revealed any differential effect of stimulus modality amongst the frontal subgroups. This is in contrast to some imaging studies which have argued that lateralisation reflects the type of material, with visual material activating the right PFC and verbal material activating the left PFC (Brewer *et al*, 1998; Golby *et al*, 2001; Kelley *et al*, 1998; Lee *et al*, 2000, 2002; Wagner *et al*, 1998b). Instead our results seemed to be more consistent with the HERA model. Our Right Lateral subgroup was impaired on several memory measures, and there

was evidence to suggest that the primary deficit in this group was at the retrieval stage. Evidence for encoding deficits in the Encoding Specificity task however were found for both the Left Lateral and the Right Lateral groups, whilst the HERA model would predict that these should be most marked in the Left Lateral group.

More recent imaging studies, discussed in the introduction, have made more detailed predictions about the role of specific subregions of the frontal lobes in memory processing. Although the lesion results reported here are obviously far less anatomically specific than findings from neuroimaging studies, some similarities and differences will be highlighted. As regards the role of the left PFC, several suggestions have been made. The left ventrolateral PFC, and the left inferior frontal gyrus in particular, has been specifically associated with semantic processing, and has variously argued to subserve retrieval of semantic information (Demb *et al*, 1995; Tulving *et al*, 1994), maintenance of semantic attributes in working memory (Gabrieli *et al*, 1998), or selection amongst competing semantic attributes (Thompson-Schill *et al*, 1997, 1999; Dolan & Fletcher, 1997; Fletcher *et al*, 2000). Alternatively the left ventrolateral PFC has been argued to be involved in cue specification at retrieval (Cabeza *et al*, 2003). The left dorsolateral PFC, on the other hand, has been argued to be specifically involved in organisation at encoding (Fletcher *et al*, 1998a, Savage *et al*, 2001), in monitoring and verification following retrieval (Dobbins *et al*, 2002; Ranaganath *et al*, 2000), or in complex heuristic retrieval processes, such as cue specification (Nolde *et al*, 1998a).

The results obtained in the Encoding Specificity task indicated that the Left Lateral PFC did have some role to play at encoding. However these encoding deficits were also found for the Right Lateral and for the Medial group, indicating that they may not be specifically left lateralised. Furthermore when analysis was restricted to those patients with damage to the left IFG, no encoding effects were found. Of course power here is reduced by the small sample sizes, but these results indicate that the left IFG may be involved, but not necessary for semantic processing at encoding.

When the specific role of the left lateral PFC was investigated in more detail, the results were mixed. Planned comparisons suggested that there may be some support for the selection hypothesis of Thompson-Schill *et al* (1997), but the strength of the results was not sufficient to draw any firm conclusions. The Left Lateral PFC (amongst other frontal regions) does seem to be involved in the use of semantics at encoding, but the present results cannot distinguish between the retrieval, maintenance or selection accounts. Indeed these accounts may prove difficult to tease apart. For example when more semantic attributes are available to choose between, more maintenance in working memory will also be required whilst they are processed. These accounts may represent a hierarchy of processing rather than regionally specific functions.

Our Left Lateral group was not large enough to separate into those with ventrolateral vs dorsolateral damage so our results cannot speak to this specific distinction. However on the basis of the results reported by Fletcher *et al* (1998a) and Savage *et al* (2001) we might have expected to find a deficit in organization at encoding amongst the Left Lateral group. However we found no difference in recall rates when stimuli were presented randomly, or when external encoding assistance was provided in the form of blocking, in either the verbal or visual OM tasks (Chapter 5). No disproportionate improvement was found in the recall of the Left Lateral group for the blocked conditions. Indeed no disproportionate improvement was found for any of the frontal subgroups, or for the frontal group as a whole. Our results do not therefore provide support for the argument that the left dorsolateral PFC is necessary for organisation at encoding.

There was also little evidence from our results to support a role for the left PFC at retrieval, either in cue specification (Cabeza *et al*, 2003, Nolde *et al*, 1998a), or in monitoring and verification (Dobbins *et al*, 2002; Ranganath *et al*, 2000). The Left Lateral group were not assisted by the provision of category cues at retrieval in the verbal OM task (Chapter 5) which would have indicated a deficit in cue specification. Neither did they show any impairments in the Reality Monitoring Task (Chapter 7) which might have been expected if this region is responsible for source retrieval and related monitoring processes. However the task employed here was specifically a reality

monitoring task, as opposed to monitoring of spatial or temporal source, and may therefore have tapped different processes to those identified in the majority of imaging studies of source monitoring. The only evidence that might have suggested a retrieval deficit in the Left Lateral group was their tendency to produce fewer correct answers and more confabulations in response to questions probing personal episodic memory in the Confabulation Battery (Chapter 4). However this could also have been due to an encoding deficit, as 3 out of 5 of the questions in this category referred to post-morbid events. Moreover this failure did not extend to questions probing other types of memory. Further research would be necessary to clarify the role of the Left Lateral PFC in this task.

With regards to the right lateral frontal lobe, the right ventrolateral PFC is widely thought to be responsible for cue specification, or setting up descriptions for retrieval. The right dorsolateral PFC on the other hand has been argued to be responsible for a general "retrieval mode" (Nyberg *et al*, 1996a; Rugg *et al*, 1997; Tulving *et al*, 1994; Wagner *et al*, 1998a), for simple reflective retrieval processes such as shifting and noting relations (Nolde *et al*, 1998a), or for monitoring and checking (Cabeza *et al*, 2003; Fletcher *et al*, 1996, 1998b; Henson *et al*, 1999b, 2000; Shallice, 2001). Our results certainly provide support for the idea that the Right Lateral PFC is involved at retrieval, most notably in the results of the Verbal OM Task discussed above. The results of this task indicate that the critical impairment in this group may have been in cue specification to start retrieval. Although in free recall this group produced significantly fewer correct recalls than Controls, when these cues were externally provided they produced a significantly larger number of extra correct recalls than Controls.

However we found no evidence of monitoring impairments in our Right Lateral group. Most strikingly, they showed no impairment on the specific monitoring measures in the verbal and visual OM tasks. Also, this group seemed to generally have a controlled responding strategy, unlike the other Frontal subgroups, in that they did not produce large numbers of new unpresented intrusions in the Encoding Specificity or Verbal OM tasks. They showed no tendency towards false positive responding in the Reality Monitoring

Task, and they produced significantly fewer confabulations in the Confabulation Battery than those without Right Lateral damage. These results taken together strongly imply that monitoring functions in this group were intact. They were able to monitor and reject non-presented semantic associates that either came to mind or were presented as lures at retrieval, and were able to avoid confabulatory responses in response to questioning. False recognition, extra-experimental intrusions and confabulation have all previously been attributed to poor monitoring at retrieval (e.g. Johnson, 1997), however none of these memory errors were present in this group (in fact they were actually preserved on these measures compared to other groups). The only type of confabulation that the Right Lateral group were prone to was in response to questions regarding orientation in time. As mentioned before, further research is necessary to replicate and clarify the Right Lateral impairment in this type of questioning.

However repetitions in recall were not examined in the experiments reported here, and this was the measure of monitoring used by Stuss *et al* (1994) when they reported monitoring impairments in right frontal patients. It is possible that the measure of monitoring employed here tapped different processes to those used before, or that the measure was simply not sensitive enough to detect monitoring impairments in the sample. Furthermore, monitoring has been particularly associated with the dorsolateral right PFC, and specifically with Brodmann area 9/46. With only 9 patients in the Right Lateral group (and data from only 7 in the Verbal OM task) we cannot be sure that every area of the Right Lateral PFC was represented. More detailed analysis of a number of patients with specific damage to Brodmann area 9/46 would be required to directly test the monitoring hypothesis.

10.1.4 Which Memory Impairments Follow Orbital Frontal Lobe Damage?

In terms of general memory performance the only task on which the Orbital group differed significantly from Controls was the Doors and People Test (Chapter 3). In this task the Orbital group (along with all the other Frontal subgroups) had significantly reduced memory performance. However the Orbital group were also significantly impaired in their verbal forgetting score. Like the Right Lateral group they lost a

significantly larger amount of verbal information over a delay than Controls, indicating either a consolidation or a retrieval deficit. This Orbital forgetting effect was corroborated by level 3 analyses, where those patients with inferior medial damage were found to have significantly worse verbal forgetting scores than those without inferior medial damage.

The most marked deficits in the Orbital group were in terms of intrusions and confabulations. In the Reality Monitoring task (Chapter 7) the Orbital group identified significantly fewer "New" words correctly, and misidentified significantly more of these words as "Imagined" than Controls, indicating a tendency towards false positive responding. They also produced significantly more intrusions than Controls in the Visual OM Task, and significantly more intrusions following prompting in the Verbal OM task (Chapter 5). The fact that these intrusions tended to be extra-list intrusions rather than prior-list intrusions indicated that the Orbital group were adopting an uncontrolled responding strategy whereby they were accepting semantic associates which came to mind as previously presented words, and intruding these into their recall. This type of error is consistent with a "gist" explanation of intrusions, whereby either encoded memory representations are too vague, containing only gist information, or the retrieval search is not focussed enough, allowing multiple traces to be accessed without adequate source specifying information (Schacter *et al*, 1998). It is also consistent with a monitoring impairment account (Johnson, 1997), in that they are unable to monitor the accompanying source details of their memories in order to reject intrusions. Either deficit would allow semantically appropriate but non-presented words to be accepted as veridical recalls. The Orbital group also produced significantly more confabulations than Controls in the Confabulation Battery (Chapter 4), and specifically produced significantly more confabulations in response to questions probing personal episodic memory and orientation in time.

One of the most striking characteristics of the Orbital group's performance on the battery was that they were preserved on all measures of executive functioning (Chapter 3), whilst all other frontal subgroups showed impairments. This result supports several previous

reports that patients with inferior medial damage are not impaired on tests of executive functioning (Stuss, 1991; Stuss *et al*, 1981, 1998, 2001a, b). It is interesting that this group were particularly prone to intrusions and confabulations, when these impairments have been specifically attributed to frontal / executive impairments. This highlights the fact that tests of executive function should not be used as the only marker of frontal dysfunction, as they are likely to measure only a selection of the functions undertaken by the frontal lobes. Moreover on the basis of this evidence it is argued that those tests used here may not tap the critical functions involved in confabulation.

10.1.5 Which Memory Impairments Follow Medial Frontal Lobe Damage?

The Medial group showed the most impairments of all the frontal subgroups. In terms of general memory performance they were impaired on several measures. They had a reduced hit rate compared to Controls in the Continuous Recognition Task (Chapter 8), and recall impairments in the Rey Complex Figure Test (Chapter 3), the Verbal and Visual OM tasks (Chapter 5) and the Encoding Specificity Task (Chapter 6). Examination of whether these memory impairments arose from encoding or retrieval deficits provided particular evidence for encoding impairments. In the Rey Complex Figure Test the Medial group had a recall impairment which on closer examination was accounted for by their poor copy score at encoding. In the Encoding Specificity Task they had reduced raw recall rates but this impairment disappeared when recall was examined only for those items correctly encoded. Both of these tasks therefore indicated encoding impairments in the Medial group. In the Verbal and Visual OM tasks they also had significantly impaired recall compared to Controls. In the verbal OM task in particular this arose from recalling a reduced number of categories from each list, and a reduced number of words per category. However in this task their recall was not affected by manipulations at encoding or at retrieval, so it was proposed that they may suffer from a more "pure" memory deficit than the Right Lateral group, possibly arising from disruption of cholinergic projections from the basal forebrain to the medial temporal lobe system.

The Medial group also had significant impairments in false recognition, intrusions and confabulations. In the Reality Monitoring Task (Chapter 7) they identified significantly fewer "New" words than Controls, and misidentified significantly more of these words as either "Heard" or "Imagined" than Controls, indicating a false recognition effect. Similarly in the Continuous Recognition Task (Chapter 8), in marked contrast to the other frontal subgroups, they showed a steep increase in their false positive rates from run to run. In the Visual OM task (Chapter 5) they produced significantly more intrusions than Controls, and in the Verbal OM task they produced significantly more intrusions after prompting than Controls. Like the Orbital group they tended to produce extra-list intrusions rather than prior-list intrusions, which implied that that prompting provoked an uncontrolled responding strategy in which they accepted semantic associates of the target words as presented items. As with the Orbital impairment, this could be argued to support either a "gist" explanation of intrusions (either through vague encoding or an unfocussed memory search; Schacter et al, 1998), or a monitoring impairment (Johnson, 1997). Finally in the Confabulation Battery (Chapter 4) they produced significantly more confabulations overall than Controls, and specifically in response to questions probing personal episodic memory, orientation in time and orientation in place.

Level 3: IMOnly Analyses:

The Orbital and Medial tendency towards intrusions and confabulations was corroborated by level 3 analyses, strengthening these findings. In the Reality Monitoring Task (Chapter 7) those patients with inferior medial damage (encompassing damage to the orbital region, the sub genu and the anterior cingulate) made significantly more "Heard said Imagined" errors than those without damage to this region, indicating a significant source monitoring deficit in this group.

Most strikingly, when performance led analysis was conducted on the results of the Confabulation Battery (Chapter 4), by identifying those patients who produced a total number of confabulations more than 2 standard deviations outside the normal range, all of them were found to have inferior medial damage. To our knowledge this is the first

time that a large series of frontal patients has been examined with respect to confabulation, and the results very strongly support an inferior medial localisation.

10.1.6 Integration of Orbital and Medial Frontal Lobe Findings with Evidence from Neuroimaging.

Imaging findings relating to the orbital and medial regions of the frontal lobes have been limited. However the reports that exist have highlighted associations between the ventromedial frontal lobe and encoding (Frey & Petrides, 2002, 2003), strategy mobilisation (Savage *et al*, 2001), reflecting on one's own mental states (Frith & Frith, 1999), and autobiographical retrieval (Graham *et al*, 2003; Maguire, 2001). The encoding impairments found in the Medial group are therefore consistent with Frey & Petrides (2002, 2003) findings. They are also consistent with Savage *et al*'s (2001) findings, in that they concluded that the ventromedial PFC was implicated in strategy mobilisation at encoding. The proposed involvement in reflecting on one's own mental states and in autobiographical memory also bear at least a surface relationship to the Orbital and Medial tendency towards misidentifying new items as imagined in the Reality Monitoring task, and towards producing high numbers of intrusions and confabulations. The ventromedial region has also been implicated in "basic feel-rightness" judgements underlying automatic rejection of retrieved memories, a failure of which would lead to confabulation (Moscovitch & Winocur, 2002).

The ventromedial frontal lobe is also posited to constitute a major component of a limbo-thalamic system underlying memory (Bachevalier & Mishkin, 1986; Petrides, 1989), via its connections to the basal forebrain. The basal forebrain provides cholinergic innervation to the hippocampus and amygdala, as well as to most of the neocortex, and there is extensive evidence that cholinergic mechanisms modulate learning and memory (Broks *et al*, 1988; Butters, 1985; Easton & Parker, 2003; Gold, 2003; Hasselmo, 1995; Irle & Markowitsch, 1987; Sarter *et al*, 2001, 2003; Thiel, 2003; Whitehouse *et al*, 1981, 1983). This may go some way to explaining the Medial memory impairments observed in the battery. Whilst some impairments seemed to be secondary to strategy impairments at encoding (in the Rey CFT and the Encoding Specificity Task) others were unaffected by

strategy manipulations and may therefore reflect deficits in core memory processes (Verbal OM task), which may arise from disruption of cholinergic projections to the hippocampus. The fact that the basal forebrain has been specifically associated with time-contextual memory recall (Fujii *et al*, 2002) is particularly intriguing given that our Orbital and Medial groups both produced confabulations in response to questions probing orientation in time in the Confabulation Battery (Chapter 4). However more imaging studies of these regions are necessary before any firm conclusions can be drawn about how they might be integrated with findings from lesion studies.

10.1.7 Comments On The Integration Of Findings From Neuropsychology And Neuroimaging

Although the integration of findings from lesion studies and from neuroimaging is an important step for research in neuroscience, a failure to find precisely the same effects using both methodologies should not be considered definitive negative evidence for the involvement of an area in a particular psychological process. There are several reasons why it is more difficult to replicate imaging results in neurological samples. One obvious example is that in lesion studies it is much more difficult to reliably separate encoding and retrieval processes than in imaging studies, where fine temporal discriminations can be made. In lesion studies assessment of both encoding and retrieval relies on measurement at retrieval. In addition it is very difficult in lesion studies to control for variables such as chronicity of damage, and exact site of injury, that may affect performance on a task. For example the brain may reorganize over time after damage, with other frontal regions compensating for damaged regions and resulting in preserved performance on a task, despite a lesion to regions identified as critical in neuroimaging. The majority of the patients in the present series were tested soon after surgery, and although this brings its own complications (in that the risk of postoperative confusion is higher), it does minimize the risk of functional reorganization. The second problem is establishing the exact site of injury in neurological patients. Precisely specifying lesion localization from clinical MRI scans is a difficult task, and not as specific as localization in fMRI studies. This means that detailed knowledge of the extent of a lesion is often lacking. Even when the extent is known, lesions rarely follow precise functional or

architectonic borders, so it is rarely possible to isolate a particular region to study specific lesion effects. Many lesions affect multiple subregions of the PFC, and even two lesions that are apparently similar may vary in their deep extent, producing different patterns of impairment. Furthermore regions distant from the lesion site may malfunction due to disruptions of connectivity. Distributed networks may be disrupted by just one lesion in one of the necessary regions. All of these reasons mean that the need to average across patients with sometimes very different lesions reduces the ability to make accurate subregional inferences about the localisation of specific functions.

So for example if imaging studies have shown the left PFC to be involved in episodic memory encoding, does the current finding that patients with left lateral frontal lesions are not impaired on most memory measures represent a failure to replicate? Does it imply that the left lateral PFC is not in fact necessary for encoding? Shallice (2003) argues that it should not. Firstly functional imaging studies have shown that many subregions of the left PFC are involved in encoding. A failure of correspondence could only be claimed if these exact regions had been studied in neurological patients. There may be separable functional encoding systems in different regions of the left PFC. For example organisation at encoding has been specifically associated with the left dorsolateral PFC, and investigation of patients with damage to this precise region would be necessary to directly test the organisation hypothesis (This same argument applies to testing of the monitoring hypothesis in patients with right dorsolateral damage, as mentioned above).

Secondly, although functional imaging studies have shown the left PFC to be more involved at encoding than retrieval, they also activate regions of the right PFC. Even if a patient had a complete lesion of the left PFC, they would still have the right PFC intact. Unilateral lesions therefore may only lead to a small drop in resources, which reduces the power of lesion studies to detect impairments. Imaging findings do not indicate that a process or function relies on one area alone, and thus cannot be used to formulate a specific hypothesis that a lesion to this area will result in complete loss of this function.

However converging findings from neuroimaging and neuropsychology are important. Using specific anatomical subgroups in lesion studies reveals important regional effects that may be masked in large groupings. And if precise hypotheses are made about the role of a particular region in a particular process lesion studies can be used to establish necessity where imaging studies only establish involvement. However at present, failures to replicate findings from imaging, when the two methodologies have such different capabilities regarding specification, should not be taken as definitive negative evidence for the involvement of a region in a particular process. Instead more lesion studies, with larger sample sizes and more specific subgroupings, are needed before drawing firm conclusions about the involvement or necessity of different regions for memory processing based on imaging results.

10.2 Which Additional Impairments Lead To Confabulation?

The presence of memory impairments in patients with frontal lobe lesions has therefore been confirmed, and some clues as to lesion-behaviour relationships have been found. However these basic impairments do not alone account for the most extreme frontal memory impairment – confabulation. The presence of confabulation was confirmed in the sample in the Confabulation Battery (Chapter 4), where we obtained striking anatomical results. All patients who produced a total number of confabulations outside the normal range had inferior medial damage. This is the first time that confabulation has been linked to specific anatomical areas in a frontal series. Because of the connections of the inferior medial region, this finding is consistent with reports that the critical lesion site for confabulation is likely to impact upon both the basal forebrain and the frontal cortex, via the anterior limbic loop connecting the amygdala, the dorsomedial nucleus and the orbitofrontal cortex (De Luca, 1993; De Luca & Cicerone, 1991; De Luca & Diamond, 1995; Fischer *et al*, 1995; Hashimoto *et al*, 2000; Irle *et al*, 1992; Schnider *et al*, 2000b; Schnider & Ptak, 1999; Treyer *et al*, 2003; Vilkki, 1985). This would indicate that confabulation arises in conjunction with a dual impairment both to core memory processes and to executive control processes overseen by the frontal lobe (although not necessarily those measured by common tests of executive function, see Chapter 3).

Consistent with previous reports, confabulation occurred most commonly in episodic memory and in orientation to time. However we reported one case of fantastic confabulation which, in breaking rules of continuity, reality and likelihood, by definition involved semantic knowledge. As we have seen, the same areas of damage associated with confabulation (Orbital and Medial) were associated with high rates of false recognition and intrusions. Although spontaneous confabulation is obviously a more extreme condition, it may involve similar processes, and similar anatomical areas, as these more basic memory impairments.

So what is the critical impairment in confabulation? One theory which was specifically explored was the temporal context confusion account proposed by Schnider and colleagues. We reported strong support for Schnider and Ptak's (1999) report of a characteristic pattern of performance on their continuous recognition task. Spontaneous confabulators do seem to show a constant hit rate accompanied by a steeply increasing false positive rate run to run. The results reported in Chapter 8 indicate that this pattern of responding is not shown by frontal patients in general, and that this task may reliably distinguish between confabulating and non-confabulating patients.

However our results did not provide support for the cognitive mechanism proposed by Schnider and colleagues to underly this pattern of performance. We found no evidence of an inability to keep memory traces out of the present. Schnider and colleagues argue that the fundamental deficit in spontaneous confabulation is "a failure to suppress evoked memories that do not pertain to ongoing reality" (Schnider, 2001, p 154). However in two experiments reported here we found no evidence that previously encountered events are experienced as having occurred more recently than they actually did. In fact if anything there was a trend in two out of three of our patients to think that events had occurred longer ago. There was also no evidence that our patients produced large numbers of previous-item intrusions in the verbal and visual organisation and monitoring tasks, which would have indicated an intrusion of inappropriate old associations into the present. Instead we found that our spontaneously confabulating patients simply have a complete inability to place remembered information in its correct temporal context.

There are four fundamental difficulties with the account of confabulation proposed by Schnider and colleagues. Firstly, their assertion that their task does not require conscious temporal discrimination processes, and that this task can distinguish between confabulating and non-confabulating amnesics, whilst traditional temporal tasks are failed by both groups, is problematic. On the basis of our results it seems that our patients simply did not have the temporal information available to them to complete the task, and that this was a sufficient explanation for their failure. With one exception (Johnson *et al*, 1997) other temporal tasks have not been used to try to distinguish between confabulating and non-confabulating patients, and this needs to be investigated. In addition specific examination of whether non-confabulating patients with temporal confusion can actually perform normally on the Schnider & Ptak (1999) task is required. If after these investigations the task is still found to reliably distinguish between confabulating and non-confabulating frontal patients, taking into account temporal confusion, it would appear a very important tool indeed for isolating the critical impairment underlying confabulation. However a clearer specification of exactly how the task is carried out in the absence of temporal awareness would then be required. On the basis of our results there is no evidence that it involves suppression of currently irrelevant items.

Secondly their assertion that suppression of associations that do not pertain to ongoing reality occurs before they reach consciousness seems improbable given that in many situations we need to have previous information and experiences consciously available to us. In many cases any monitoring or choosing between stimuli needs to be done consciously on the basis of current demands. It seems more likely that the early activation reported by Schnider *et al* (2003) in association with correct rejection of currently irrelevant items might reflect some kind of temporal tagging of information as "past", which can be later used for monitoring according to the task requirements.

However even if these theoretical points are addressed, two more general problems remain. An account such as Schnider's cannot explain single content-specific confabulations such as that reported by Burgess & McNeil (1999), as general temporal confusion would be expected to have a general effect. Secondly, it cannot explain bizarre

and fantastic confabulations such as those produced by patient 143, or confabulations in the semantic domain. Even though a confusion of temporal source or current relevance may play some part, it cannot explain how such bizarre ideas arise in the first place, and are accepted as reality. One clue to a further mechanism that may contribute to the production of confabulatory ideas was provided by our patients' performance on the reality monitoring task. This suggested that confabulating patients may have difficulty in identifying the nature of an experience, and that in some cases (2 out of 3 of our patients) this may take the form of a bias to misidentify imagined events as real (interestingly this was not a general Frontal phenomenon). If the confusions suffered by confabulators not only encompass mixing up events in time, but also mixing up reality and imaginings, then confabulations such as those produced by patient 143 are more explicable.

We would argue that confabulation involves a combination of difficulties, including deficits in the availability of, or monitoring of, all types of information; temporal, spatial, and internal/external, in combination with a breakdown in plausibility judgements that allow fantastic ideas to be accepted as real. Six theories of confabulation, broadly grouped into "Source and Temporal Memory Deficit Theories" and "Retrieval Process Theories" were discussed in Chapter 1. Although the investigations in this thesis were not aimed at explicit testing of all of them, some comments on how they may fit with the present results will be presented.

The work of Johnson and colleagues on source and reality monitoring (Johnson, 1997, Johnson *et al*, 1993, 1997) has important links with confabulation and has been incorporated into many other theories. The results presented in Chapter 8 imply that reality monitoring, and confusion of internally and externally derived experiences may play an important role in at least some cases. We would also agree that temporal confusion is a contributing feature of confabulation. However, as previously discussed, the major problem facing source and temporal theories is that they are unable to provide a full explanation of confabulation in that they cannot explain why unusual ideas arise in the first place. It seems unlikely that most of us have to consciously assess ideas such having met someone with the head of a bee for their perceptual, temporal and contextual

features before we reject them. Whilst source and temporal memory accounts are good at explaining memory distortions similar to those that normal subjects experience everyday, they are less equipped to account for the extremes of confabulation. Dalla Barba's (1999, 2001) theory is an intriguing account in that it attempts to go beyond simple temporal judgments to introduce the role of consciousness in confabulation. However as yet the individual processes and functions involved in Temporal Consciousness and Knowing Consciousness are not clearly specified enough to be tested. As discussed above, Schnider and colleagues have provided a task which seems to provide striking results which may be specific to spontaneous confabulators. However suppression of inappropriate associations seems not to be the fundamental deficit explaining performance on this task, and further investigation is needed to clarify a) if the task truly distinguishes between confabulating and non-confabulating patients with temporal confusion, and b) how the task is carried out in the absence of temporal knowledge.

At present it appears that the accounts most likely to offer a full explanation of confabulation are those which incorporate source and temporal memory difficulties into general accounts of retrieval. These "two factor" theories attempt to account for the production of bizarre ideas in the first place and for subsequent monitoring failures (temporal or otherwise) which allow them to be accepted as veridical. Burgess & Shallice (1996), Conway & Tacchi (1996), Kopelman (1999), Moscovitch (1982, 1992, 1995, Moscovitch & Melo, 1997), Norman & Schacter (1996) and Schacter *et al* (1998) all highlight a) an inability to organise and initiate an appropriate search in long-term memory, and b) a subsequent inability to monitor and evaluate the products of this search which allow memories that are incorrect either in content or in context to be accepted as appropriate.

Evidence that our three confabulators were impaired at organising and initiating an appropriate search in memory was provided by their performance on the Verbal OM Task, where they showed marked improvements in their rates of correct recall when external retrieval cues were provided in the form of category names. This presumably overcame their inability to produce appropriate retrieval cues themselves. The fact that

this manipulation also led to increased rates of intrusions provides some support for the presence of an additional monitoring or criterion setting deficit, in that they are unable to reject incorrect but semantically related items retrieved along with target items. Our specific monitoring measure (where subjects were required to indicate repeated words) supported a monitoring deficit in the verbal OM task, in that the confabulators were over-inclusive in their monitoring, tending to identify new words as repeated as well (although this pattern was not present in the visual OM task). There was also some evidence to support Moscovitch's proposal that strategic retrieval processes should be more impaired than associative or cue-dependent retrieval processes, as these patients were more consistently impaired on recall than recognition tasks. Retrieval accounts therefore seem to fit well with the data reported here.

Retrieval accounts are likely to be fruitful in developing models of confabulation. However they are not without their problems. One problem is that at present the first factor, the search in memory which produces confabulatory ideas in the first place, is rather poorly specified. Moscovitch's (1995) associative cue-dependent retrieval system and Schacter *et al*'s (1998) "focusing of the retrieval search" explanations do not readily account for the production of bizarre and fantastic ideas. Why is the output in these cases so faulty? Burgess & Shallice's (1996) account of descriptor processes is better specified, but is still very difficult to isolate in order to test explicitly in confabulating patients. In general these accounts more readily explain normal everyday memory errors than bizarre and fantastic confabulations.

The second problem is with the concept of monitoring. Several authors have pointed out the logical difficulty of identifying what or who is doing the monitoring (Dalla Barba, 2001; Schacter *et al*, 1998; Ward, 2003). If monitoring is a conscious process then we should all be consciously aware of rejecting ideas such as those produced by confabulating patients. We know from experience that this is not true. However if the monitoring process is unconscious, who is doing it? As Dalla Barba (2001) points out, this raises the problem of the homunculus. There is also the question of identifying the criteria by which we might monitor our memories. The only information that monitoring

can be based on is that which cue specification is also based on. Therefore Schacter *et al* (1998) have argued against the separation of these processes. Dalla Barba (2001) also asks why we should trust perceptual or contextual memories which are retrieved in association with a target memory if we do not trust the target memories themselves? It is easy for the concept of monitoring to become circular. However retrieval process theories seem currently to be the most promising methods of explaining both confabulation and normal memory retrieval and its errors. Further investigation from both neuroimaging and neuropsychology, and emerging findings from the study of consciousness, are likely to refine them even further.

Most accounts of confabulation have focused on deficits at the retrieval stage, as patents tend to confabulate about premorbid events as well as postmorbid ones. Fukatsu, Yamadori & Fujii (1998) have provided explicit evidence that encoding was not impaired in their basal forebrain amnesia patients as the patient recovered five weeks post-incident, and was able to recall events that had occurred during the postictal amnesic phase after recovery. This pattern strongly suggests that his impairment was solely at the retrieval stage, and this has been reported before (Diamond *et al*, 1997). However there was some evidence in our Medial patients for difficulties at the encoding stage as well. Whilst this may not be the core impairment in confabulation, encoding deficits may also play a role, especially given that memory is likely to be affected by repeated retrieval / encoding cycles. Schacter *et al* (1998), for example, in their constructive memory framework, incorporate ideas of feature binding and pattern separation at encoding which may account for some instances of confabulation.

Confabulation is likely to involve many disparate deficits in memory processing. The subjective quality of memories appears changed in some way, either though changes at encoding or at retrieval, so that memories are vague and confused, lacking in clarity or supporting detail, and mixed up with imaginings and ideas. Distinguishing between these fragments is then difficult. Memory control processes are disrupted, so that patients cannot monitor and verify the thoughts that enter consciousness. They may also be suffering temporal confusion and reality monitoring difficulties in identifying the source

of a thought or idea or experience. All of these elements are inevitably tied up with the "self", the personality and motivations of the individual, which will determine the particular ideas that arise. However the subjective experience of confabulation, the conviction that patients exhibit that their memories are true, and their inability to use logic to dismiss bizarre ideas, is possibly the most difficult factor to explain. This is where confabulation steps outside the realm of normal experience, and when it becomes less easy to accommodate in theories of normal memory and normal memory errors. Findings from the emerging study of consciousness are likely to provide the greatest contribution to theories of confabulation in this regard.

10.3 Conclusions

This thesis has presented the results of a large scale clinical series investigating memory performance and confabulation in a sample of patients with focal frontal lobe lesions. Its main contribution has been the use of new methodological approaches in an attempt to more clearly specify lesion-behaviour relationships within the frontal lobes. The use of two detailed methods of analysis allowing comparison of patients with lesions in specific areas to others has revealed different patterns of impairment in association with different lesion sites. Patients behave differently depending on the site of their lesion. This methodology represents an important step forward in neuropsychological research. The use of undifferentiated frontal groups can conceal effects that are actually present in subgroups of the sample, or create contradictory results when different studies contain a different balance of lesion sites, for example through biases towards the use of particular aetiologies. The use of performance led analysis (which revealed the inferior medial effect in confabulation in Chapter 4), and the ability to analyse only those with damage to very specific regions of the frontal lobes (for example analysis of patients with left inferior frontal gyrus lesions in Chapter 6) have allowed even more detailed conclusions to be drawn. The main problem with this approach of course is the small sample sizes that result from subdividing groups of patients who are already scarce. However, even taking this into account, the lesion specificity approach appears to be a very effective method for the study of brain-behaviour relationships.

A further contribution of the work presented here, and the use of the lesion specificity approach, has been the ability to directly compare results from neuroimaging and neuropsychology, including in one case a direct test of imaging results using the same methodology (Chapter 6). This comparison has revealed important converging findings. Most notably patients with Right Lateral frontal damage showed memory impairments that are consistent with deficits at the retrieval stage. This is the first report of lesion evidence in support of imaging evidence linking the right lateral PFC to retrieval operations. This is also the first study to investigate confabulation in a general frontal sample, and confirm previous hypotheses of an association between confabulation and damage to the Orbital and Medial regions of the frontal lobe.

Finally this thesis has presented the first direct test of the suppression hypothesis of confabulation proposed by Schnider and colleagues. Our results confirm the effectiveness of their continuous recognition task. It is a powerful test that may distinguish between confabulating and non-confabulating patients. However the fundamental deficit underlying the characteristic pattern of performance on this task, on the basis of the results reported here, appears not to be a failure to suppress inappropriate activations. Further specification of the mechanisms involved in this task is required.

The results reported here have also raised several important future directions for research. The first is the critical importance of connectivity effects in investigating brain-behaviour relationships. The presence of confabulation in this sample was associated with Orbital and Medial frontal lobe damage. However it is associated with control processes that have been attributed to the lateral frontal lobes in imaging studies (for example monitoring and cue specification). Further investigation of how the Medial and Orbital frontal lobe may interact with more lateral cortical regions is a critical area for future research. Further imaging studies of the Medial and Orbital frontal lobe are also critical to specify the involvement of these regions in normal memory processing. This is one area where evidence from lesion studies is at present more advanced than that from neuroimaging. As new methods are developed to overcome the artefacts involved in

imaging these regions, neuroimaging studies are likely to provide important information about the roles of these regions in memory processing and confabulation.

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APPENDIX 1: Baseline Assessments: Insignificant Analyses

Level 1 Analyses

Ref		ANOVA / Kruskal Wallis result
1.1	Stroop Word Score	$F_{(2, 92)} = 1.22$, $p = 0.30$
1.2	Stroop Word Errors	$F_{(2, 92)} = 0.41$, $p = 0.66$
1.3	Stroop Colour –Word Errors	$\chi^2 = 1.04$, $df = 2$, $p = 0.60$
1.4	Trails A Errors	$F_{(2, 95)} = 2.28$, $p = 0.11$
1.5	Trails B Errors	$F_{(2, 93)} = 0.79$, $p = 0.46$
1.6	FAS Errors	$F_{(2, 94)} = 0.17$, $p = 0.84$
1.7	Story Recall Intrusions In Immediate Recall	$\chi^2 = 2.77$, $df = 2$, $p = 0.25$
1.8	Story Recall Intrusions In Delayed Recall	$F_{(2, 96)} = 2.52$, $p = 0.09$
1.9	Story Recall Retained Percentage	$\chi^2 = 2.43$, $df = 2$, $p = 0.30$
1.10	Rey Copy Score	$F_{(2, 99)} = 2.11$, $p = 0.13$
1.11	Rey Good Continuation Score	$F_{(2, 98)} = 2.29$, $p = 0.11$
1.12	Rey Strategy Score	$F_{(2, 98)} = 1.93$, $p = 0.15$

Level 2 Analyses

Ref		Orbital Mean (SD)	Medial Mean (SD)	Left Lateral Mean (SD)	Right Lateral Mean (SD)	Control Mean (SD)	ANOVA / Kruskal Wallis result
2.1	Ravens APM Scaled Score	10.92 (2.27	8.13 (3.68)	9.22 (1.48)	9.89 (3.86)	11.18 (2.85)	$F_{(4, 81)} = 2.49$, $p = 0.06$
2.2	NART FSIQ	105.73 (10.15)	96.50 (16.29)	108.38 (18.72)	112.00 (12.91)	110.64 (9.78)	$\chi^2 = 8.36$, $df = 4$, $p = 0.08$
2.3	GNT Scaled Score	9.18 (3.89)	8.71 (3.20)	11.22 (2.77)	10.88 (3.64)	11.04 (3.49)	$F_{(4, 78)} = 1.51$, $p = 0.21$
2.4	Incomplete Letters	19.64 (0.50)	18.63 (2.00)	19.11 (1.05)	19.25 (0.71)	19.26 (0.88)	$F_{(4, 79)} = 0.75$, $p = 0.56$
2.5	Stroop Word Score	112.00 (0.00)	106.86 (13.61)	112.00 (0.00)	111.25 (2.12)	111.96 (0.20)	$\chi^2 = 3.40$, $df = 4$, $p = 0.49$
2.6	Stroop Word Errors	0.00 (0.00)	0.14 (0.38)	0.00 (0.00)	0.00 (0.00)	0.06 (0.24)	$F_{(4, 74)} = 0.57$, $p = 0.68$
2.7	Stroop Colour-Word Errors	2.89 (6.99)	0.00 (0.00)	6.14 (13.21)	10.86 (19.42)	1.02 (1.98)	$\chi^2 = 6.17$, $df = 4$, $p = 0.19$
2.8	Trails A Errors	0.27 (0.47)	0.38 (0.52)	0.00 (0.00)	0.25 (0.71)	0.16 (0.42)	$F_{(4, 77)} = 0.65$, $p = 0.63$
2.9	Trails B Errors	1.27 (3.26)	0.29 (0.49)	0.86 (1.46)	0.63 (0.74)	0.44 (0.61)	$F_{(4, 76)} = 0.46$, $p = 0.77$
2.10	FAS Errors	2.78 (2.49)	1.13 (1.25)	1.50 (1.31)	1.38 (1.69)	1.64 (1.68)	$F_{(4, 76)} = 1.40$, $p = 0.24$
2.11	Proverbs	1.20 (0.52)	1.03 (0.35)	1.11 (0.37)	1.21 (0.32)	1.39 (0.28)	$F_{(4, 77)} = 2.32$, $p = 0.07$

2.12	Famous Faces Correct	9.27 (2.05)	9.25 (3.28)	9.89 (2.03)	10.29 (2.06)	10.31 (2.00)	$F_{(4, 78)} = 0.80, p = 0.53$
2.13	Story Recall Immediate Recall Score	35.91 (15.79)	31.38 (7.87)	31.75 (12.63)	31.44 (13.33)	10.31 (2.00)	$F_{(4, 79)} = 2.30, p = 0.07$
2.14	Story Recall Intrusions Immediate Recall	1.00 (1.67)	1.75 (2.31)	0.50 (0.76)	0.78 (0.97)	0.86 (1.20)	$F_{(4, 79)} = 0.85, p = 0.50$
2.15	Story Recall Delayed Recall Score	31.18 (17.35)	27.38 (8.73)	30.00 (11.66)	28.56 (16.13)	35.76 (8.89)	$F_{(4, 79)} = 2.22, p = 0.07$
2.16	Story Recall Intrusions Delayed Recall	1.91 (2.39)	2.13 (2.90)	0.75 (0.71)	0.33 (0.50)	1.32 (1.28)	$F_{(4, 79)} = 2.31, p = 0.07$
2.17	Story Recall Retained Percentage	75.82 (36.94)	85.88 (13.30)	97.13 (15.61)	81.39 (30.88)	92.44 (11.94)	$\chi^2 = 5.46, df = 4, p = 0.24$
2.18	Rey Good Continuation Score	13.36 (2.73)	10.88 (5.30)	13.29 (4.11)	12.78 (3.42)	12.98 (2.98)	$F_{(4, 78)} = 0.82, p = 0.52$
2.19	Rey Symmetry Score	8.09 (4.04)	7.63 (4.78)	7.86 (4.30)	6.44 (4.25)	9.64 (4.53)	$F_{(4, 78)} = 1.34, p = 0.26$
2.20	Rey Strategy Score	21.45 (5.91)	18.50 (8.94)	21.14 (7.01)	19.22 (3.55)	22.62 (6.46)	$F_{(4, 78)} = 1.05, p = 0.39$

Ref 2.21

Famous Faces False Recognition (Frontal Subgroup x Famous / Unknown Faces) ANOVA

	Orbital Mean (SD)	Medial Mean (SD)	L Lateral Mean (SD)	R Lateral Mean (SD)	Control Mean (SD)
Incorrect Responses to Famous Faces					
Incorrect Responses to Unknown Faces					

Frontal Subgroup	$F_{(1, 78)} = 2.43, p = 0.06$
Stimulus Type (Famous vs Unknown Faces)	$F_{(1, 78)} = 2.08, p = 0.15$
Frontal Subgroup x Stimulus Type Interaction	$F_{(4, 78)} = 1.27, p = 0.29$

Level 3 Analyses (Reported only following a significant level 1 analysis)

SMIM

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
3.1	Ravens APM	N = 13 8.76 (2.59)	N = 27 9.29 (3.60)	$T_{(38} = 0.47, p = 0.64$
3.2	Stroop Word Time	N = 11 79.91 (38.66)	N = 22 68.63 (25.21)	$T_{(31)} = -1.01, p = 0.32$
3.3	Trails A Time	N = 11 52.45 (35.02)	N = 25 54.88 (34.56)	$T_{(34)} = 0.19, p = 0.85$
3.4	Trails B Time	N = 10 119.10 (68.14)	N = 24 139.70 (115.67)	$T_{(32)} = 0.52, p = 0.60$
3.5	Elevator subtest (TEA)	N = 12 5.58 (1.62)	N = 25 6.44 (1.19)	$T_{(35)} = 1.82, p = 0.08$
3.6	RMT Words	N = 12 43.50 (4.85)	N = 27 42.59 (8.12)	$T_{(37)} = -0.36, p = 0.72$
3.7	RMT Faces	N = 12 37.75 (13.62)	N = 27 41.18 (7.50)	$T_{(37)} = 1.02, p = 0.32$
3.8	Story Recall Immediate Recall Score	N = 12 30.08 (10.90)	N = 26 31.12 (13.68)	$T_{(36)} = 0.23, p = 0.82$
3.9	Story Recall Delayed Recall Score	N = 12 25.67 (12.48)	N = 26 28.08 (14.06)	$T_{(36)} = 0.51, p = 0.62$
3.10	Rey Copy Time	N = 10 228.80 (87.97)	N = 18 226.78 (97.62)	$T_{(26)} = -0.05, p = 0.96$
3.11	Rey Delayed Recall Score	N = 12 11.91 (5.82)	N = 23 13.00 (8.06)	$T_{(33)} = 0.41, p = 0.68$
3.12	Doors & People People Subtest (Verbal Recall)	N = 11 9.18 (4.40)	N = 24 7.33 (2.68)	$T_{(33)} = -1.54, p = 0.13$
3.13	Doors and People Doors Subtest (Visual Recognition)	N = 12 8.08 (3.00)	N = 24 8.79 (3.30)	$T_{(34)} = 0.63, p = 0.54$
3.14	Doors & People Shapes Subtest (Visual Recall)	N = 12 7.75 (4.18)	N = 24 8.29 (3.92)	$T_{(34)} = 0.38, p = 0.70$
3.15	Doors & People Names Subtest (Verbal Recognition)	N = 11 8.45 (4.41)	N = 24 8.75 (3.55)	$T_{(33)} = 0.21, p = 0.83$

IMOnly

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
4.1	Ravens APM	N = 18 8.89 (3.51)	N = 22 9.32 (3.15)	$T_{(38)} = 0.41$, $p = 0.69$
4.2	Stroop Word Time	N = 14 65.93 (25.23)	N = 19 77.16 (33.28)	$T_{(31)} = 1.06$, $p = 0.30$
4.3	Trails A Time	N = 16 56.25 (38.11)	N = 20 52.45 (31.67)	$T_{(34)} = -0.33$, $p = 0.75$
4.4	Trails B Time	N = 15 141.93 (122.10)	N = 19 127.11 (88.81)	$T_{(32)} = -0.41$, $p = 0.68$
4.5	Elevator subtest (TEA)	N = 17 6.29 (1.36)	N = 20 6.05 (1.43)	$T_{(35)} = -0.53$, $p = 0.60$
4.6	RMT Words	N = 18 42.06 (8.52)	N = 21 43.57 (6.02)	$T_{(37)} = 0.65$, $p = 0.52$
4.7	RMT Faces	N = 18 40.28 (8.37)	N = 21 40.00 (10.97)	$T_{(37)} = -0.09$, $p = 0.93$
4.8	Story Recall Immediate Recall Score	N = 17 30.29 (13.31)	N = 21 31.19 (12.56)	$T_{(36)} = 0.21$, $p = 0.83$
1.9	Story Recall Delayed Recall Score	N = 17 26.35 (12.70)	N = 21 28.09 (14.30)	$T_{(36)} = 0.39$, $p = 0.70$
4.10	Rey Copy Time	N = 12 218.00 (106.57)	N = 16 234.63 (83.61)	$T_{(26)} = 0.46$, $p = 0.65$
4.11	Rey Delayed Recall Score	N = 17 12.97 (7.80)	N = 18 12.31 (6.99)	$T_{(33)} = -0.27$, $p = 0.79$
4.12	Doors & People People Subtest (Verbal Recall)	N = 16 7.37 (2.68)	N = 19 8.37 (3.86)	$T_{(33)} = 0.87$, $p = 0.39$
4.13	Doors and People Doors Subtest (Visual Recognition)	N = 16 8.88 (3.52)	N = 20 8.30 (2.94)	$T_{(34)} = -0.53$, $p = 0.60$
4.14	Doors & People Shapes Subtest (Visual Recall)	N = 16 8.13 (4.00)	N = 20 8.10 (4.02)	$T_{(34)} = -0.02$, $p = 0.99$
4.15	Doors & People Names Subtest (Verbal Recognition)	N = 16 8.06 (2.91)	N = 19 9.16 (4.40)	$T_{(33)} = 0.85$, $p = 0.40$

LLat

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
5.1	Ravens APM	N = 14 8.29 (3.27)	N = 26 9.58 (3.26)	$T_{(38)} = 1.19$, $p = 0.24$
5.2	Stroop Word Time	N = 13 69.08 (27.52)	N = 20 74.55 (32.36)	$T_{(31)} = 0.50$, $p = 0.62$
5.3	Trails A Time	N = 12 55.00 (35.01)	N = 24 53.71 (34.56)	$T_{(34)} = -0.11$, $p = 0.92$
5.4	Trails B Time	N = 11 174.00 (135.94)	N = 23 114.35 (80.13)	$T_{(32)} = -1.61$, $p = 0.12$
5.5	Elevator subtest (TEA)	N = 13 6.00 (1.47)	N = 6.25 (1.36)	$T_{(35)} = 0.52$, $p = 0.61$
5.6	RMT Words	N = 13 41.92 (7.69)	N = 26 43.34 (7.08)	$T_{(37)} = 0.58$, $p = 0.57$
5.7	RMT Faces	N = 13 39.08 (8.68)	N = 26 40.65 (10.34)	$T_{(37)} = 0.47$, $p = 0.64$
5.8	Story Recall Immediate Recall Score	N = 13 30.23 (14.56)	N = 25 31.08 (11.98)	$T_{(36)} = 0.19$, $p = 0.85$
5.9	Story Recall Delayed Recall Score	N = 13 27.92 (13.59)	N = 25 27.00 (13.66)	$T_{(36)} = -0.20$, $p = 0.85$
5.10	Rey Copy Time	N = 10 194.80 (69.77)	N = 18 245.67 (100.36)	$T_{(26)} = 1.42$, $p = 0.17$
5.11	Rey Delayed Recall Score	N = 12 15.00 (7.19)	N = 23 11.39 (7.19)	$T_{(33)} = -1.41$, $p = 0.17$
5.12	Doors & People People Subtest (Verbal Recall)	N = 12 8.25 (3.86)	N = 23 7.74 (3.15)	$T_{(33)} = -0.42$, $p = 0.68$
5.13	Doors and People Doors Subtest (Visual Recognition)	N = 12 8.00 (3.67)	N = 24 8.83 (2.94)	$T_{(34)} = 0.74$, $p = 0.46$
5.14	Doors & People Shapes Subtest (Visual Recall)	N = 12 9.08 (5.18)	N = 24 7.63 (3.20)	$T_{(34)} = -1.04$, $p = 0.30$
5.15	Doors & People Names Subtest (Verbal Recognition)	N = 12 7.67 (3.96)	N = 23 9.17 (3.66)	$T_{(33)} = 1.12$, $p = 0.27$

RLat

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
6.1	Ravens APM	N = 13 9.69 (3.25)	N = 27 8.85 (3.32)	$T_{(38)} = -0.75$, $p = 0.45$
6.2	Stroop Word Time	N = 11 69.91 (24.56)	N = 22 73.64 (33.16)	$T_{(31)} = 0.33$, $p = 0.74$
6.3	Trails A Time	N = 12 49.08 (27.65)	N = 24 56.67 (37.36)	$T_{(34)} = 0.62$, $p = 0.54$
6.4	Trails B Time	N = 12 128.08 (100.46)	N = 22 136.68 (107.11)	$T_{(34)} = 0.23$, $p = 0.82$
6.5	Elevator subtest (TEA)	N = 12 6.08 (1.51)	N = 25 6.20 (1.35)	$T_{(35)} = 0.24$, $p = 0.81$
6.6	RMT Words	N = 13 44.15 (6.40)	N = 26 42.23 (7.63)	$T_{(37)} = -0.78$, $p = 0.44$
6.7	RMT Faces	N = 13 42.15 (4.91)	N = 26 39.12 (11.37)	$T_{(36.54)} = -1.16$, $p = 0.25$
6.8	Story Recall Immediate Recall Score	N = 13 33.31 (12.66)	N = 25 29.48 (12.82)	$T_{(36)} = -0.88$, $p = 0.39$
6.9	Story Recall Delayed Recall Score	N = 13 29.92 (14.32)	N = 25 25.96 (13.08)	$T_{(36)} = -0.86$, $p = 0.40$
6.10	Rey Copy Time	N = 9 227.22 (102.37)	N = 19 227.63 (90.63)	$T_{(26)} = 0.01$, $p = 0.99$
6.11	Rey Delayed Recall Score	N = 11 13.09 (7.55)	N = 24 12.42 (7.33)	$T_{(33)} = -0.25$, $p = 0.80$
6.12	Doors & People People Subtest (Verbal Recall)	N = 12 9.41 (3.58)	N = 24 7.13 (3.03)	$T_{(33)} = -1.99$, $p = 0.06$
6.13	Doors and People Doors Subtest (Visual Recognition)	N = 12 8.91 (2.87)	N = 24 8.38 (3.36)	$T_{(34)} = -0.48$, $p = 0.64$
6.14	Doors & People Shapes Subtest (Visual Recall)	N = 12 8.33 (3.26)	N = 24 8.00 (4.32)	$T_{(34)} = -0.24$, $p = 0.82$
6.15	Doors & People Names Subtest (Verbal Recognition)	N = 12 10.42 (4.72)	N = 23 7.74 (2.90)	$T_{(15.49)} = -1.80$, $p = 0.09$

APPENDIX 2: Confabulation Battery

General Semantic Memory.
1. What happened to President Kennedy?
2. Who is John Major?
3. Who is Terry Wogan?
4. What happened in the Falklands?
5. Who were the Beatles?

Personal Semantic Memory.
1. Tell me about the street that you live in
2. Do you have any brothers or sisters?
3. What was your father's job?
4. What is your job?
5. What kind of education or training have you completed?

Personal Episodic Memory.
1. What did you eat for breakfast this morning?
2. What did you do yesterday?
3. What kind of treatments have you had here?
4. How did you spend last Christmas?
5. Have you been to this hospital before?

Orientation in Time.
1. What year is it?
2. What season are we in?
3. What month is it?
4. What is the date?
5. What time is it?

Orientation to Place.
1. Where are we now?
2. Which floor is your ward on?
3. Which city are we in?
4. Which is the nearest tube station?
5. What is your home address?

Don't Know
1. Who is the current world-fencing champion?
2. Who is Stockhausen?
3. Who was the author of Black Snow?
4. How long is the river Boas?
5. Who invented the electric iron?

Mythological Question.
1. Tell me the story of Red Riding Hood

APPENDIX 3: Confabulation Battery: Insignificant Analyses

Level 1 Analyses

Ref		Frontal Mean (SD)	Posterior Mean (SD)	Control Mean (SD)	Kruskal Wallis Result
1.1	General Semantic Memory - Correct	4.76 (0.63)	4.75 (0.62)	4.80 (0.49)	$\chi^2 = 0.01$, df = 2, p = 0.99
1.2	General Semantic Memory - Confabulations	0.15 (0.49)	0.08 (0.29)	0.10 (0.36)	$\chi^2 = 0.21$, df = 2, p = 0.90
1.3	Personal Semantic Memory - Correct	4.84 (0.44)	4.75 (0.87)	4.98 (0.14)	$\chi^2 = 4.11$, df = 2, p = 0.13
1.4	Personal Semantic Memory - Confabulations	0.13 (0.41)	0.08 (0.29)	0.00 (0.00)	$\chi^2 = 5.31$, df = 2, p = 0.07
1.5	Orientation to Place - Correct	4.47 (0.89)	4.75 (0.62)	4.80 (0.40)	$\chi^2 = 0.012$, df = 2, p = 0.99
1.6	Orientation to Place - Confabulations	0.45 (0.86)	0.17 (0.58)	0.12 (0.33)	$\chi^2 = 5.35$, df = 2, p = 0.07
1.7	Don't Know - Correct	0.16 (0.37)	0.08 (0.29)	0.22 (0.42)	$\chi^2 = 1.41$, df = 2, p = 0.49
1.8	Don't Know - Confabulations	0.21 (0.41)	0.00 (0.00)	0.16 (0.37)	$\chi^2 = 2.98$, df = 2, p = 0.23
1.9	Little Red Riding Hood - Correct	0.61 (0.50)	0.75 (0.45)	0.74 (0.44)	$\chi^2 = 2.04$, df = 2, p = 0.36
1.10	Little Red Riding Hood - Confabulations	0.23 (0.43)	0.00 (0.00)	0.10 (0.30)	$\chi^2 = 5.52$, df = 2, p = 0.06

Level 2 Analyses

Ref		Orbital Mean (SD)	Medial Mean (SD)	Left Lateral Mean (SD)	Right Lateral Mean (SD)	Control Mean (SD)	Kruskal Wallis Result
2.1	General Semantic Memory - Correct	4.64 (0.67)	5.00 (0.00)	4.88 (0.35)	5.00 (0.00)	4.80 (0.49)	$\chi^2 = 4.17$, df = 4, p = 0.38
2.2	General Semantic Memory - Confabulations	0.18 (0.60)	0.00 (0.00)	0.13 (0.35)	0.00 (0.00)	0.10 (0.36)	$\chi^2 = 1.59$, df = 4, p = 0.81
2.3	Personal Semantic Memory - Correct	4.73 (0.65)	4.88 (0.35)	5.00 (0.00)	5.00 (0.00)	4.98 (0.14)	$\chi^2 = 7.04$, df = 4, p = 0.13
2.4	Personal Semantic Memory - Confabulations	0.27 (0.65)	0.13 (0.35)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	$\chi^2 = 10.98$, df = 4, p = 0.03 (Corrected significance level p = 0.013)
2.5	Don't Know - Correct	0.18 (0.40)	0.13 (0.35)	0.25 (0.46)	0.14 (0.38)	0.22 (0.42)	$\chi^2 = 0.68$, df = 4, p = 0.95
2.6	Don't Know - Confabulations	0.36 (0.50)	0.13 (0.35)	0.25 (0.46)	0.14 (0.38)	0.16 (0.37)	$\chi^2 = 2.91$, df = 4, p = 0.57
2.7	Little Red Riding Hood - Correct	0.45 (0.52)	0.63 (0.52)	0.75 (0.46)	0.86 (0.38)	0.74 (0.44)	$\chi^2 = 4.63$, df = 4, p = 0.33
2.8	Little Red Riding Hood - Confabulations	0.36 (0.50)	0.25 (0.46)	0.00 (0.00)	0.14 (0.38)	0.10 (0.30)	$\chi^2 = 7.13$, df = 4, p = 0.13

APPENDIX 4: Verbal Organisation and Monitoring Test Stimuli.

LIST ONE	BLOCKED	LIST FOUR	RANDOM
Ruby		Lawyer	
Emerald	Predicted Intrusions:	Pea	Predicted Intrusions:
Sapphire	Dog	Drum	Doctor
Pearl	Diamond	Teacher	Piano
Cat	Chair	Red	Carrot
Horse	Leg	Dentist	Blue
Cow		Corn	
Lion		Green	Bean
Table		Trumpet	Potato
Bed		Engineer	Yellow
Sofa		Black	Orange
Desk		Tomato	
Arm		Violin	
Head		Purple	
Eye		Lettuce	
Foot		Clarinet	

LIST TWO	RANDOM	LIST FIVE	BLOCKED
Minute		Tulip	
Ruby	Predicted Intrusions:	Carnation	Predicted Intrusions:
Uncle	Hour	Daisy	Rose
Table	Chair	Violet	Fly
Emerald	Diamond	Lawyer	Doctor
Second	Aunt	Teacher	Piano
Father		Professor	
Bed	Sapphire	Carpenter	Dentist
Mother	Pearl	Drum	Engineer
Lamp	Sofa	Trumpet	Violin
Opal	Desk	Flute	Clarinet
Year		Guitar	
Brother		Ant	
Day		Bee	
Jade		Mosquito	
Couch		Spider	

LIST THREE	BLOCKED	LIST SIX	RANDOM
Pea		Bus	
Corn	Predicted Intrusions:	Tulip	Predicted Intrusions:
Bean	Carrot	Door	Car
Potato	Blue	Ant	Window
Uncle	Aunt	Carnation	Rose
Father	Hour	Roof	Fly
Sister		Plane	
Cousin	Mother	Orchid	Daisy
Red	Brother	Bee	Violet
Green	Year	Wall	Mosquito
Yellow	Day	Train	Spider
Orange		Floor	
Minute		Beetle	
Second		Chrysanthemum	
Century		Truck	
Month		Roach	

APPENDIX 5: Verbal Organisation and Monitoring Test: Insignificant Analyses

Level 1 Analyses

Ref		ANOVA result
1.1	**List Organisation x Intrusion Type x Group ANOVA**	
	List Organisation x Intrusion Type Interaction	$F_{(1, 92)} = 0.32$, $p = 0.57$
	List Organisation x Group Interaction	$F_{(2, 92)} = 1.10$, $p = 0.34$
	Intrusion Type x Group Interaction	$F_{(2, 92)} = 1.09$, $p = 0.34$
	List Organisation x Intrusion Type x Group Interaction	$F_{(2, 92)} = 0.43$, $p = 0.65$

Level 2 Analyses

Ref 2.1: Intrusion Type x List Organisation x Frontal Subgroup ANOVA

	Orbital Mean (SD)	Medial Mean (SD)	L Lateral Mean (SD)	R Lateral Mean (SD)	Control Mean (SD)
Mean Extra-List Intrusions					
Blocked Lists	0.73 (0.92)	0.71 (0.45)	0.46 (0.56)	0.33 (0.27)	0.50 (0.71)
Random Lists	0.30 (0.35)	0.33 (0.38)	0.38 (0.42)	0.10 (0.16)	0.23 (0.30)
Mean Prior-List Intrusions					
Blocked Lists	0.50 (0.55)	1.43 (1.48)	1.0 (2.04)	0.43 (0.53)	0.73 (0.84)
Random Lists	0.33 (0.33)	0.62 (0.59)	0.75 (0.77)	0.52 (0.69)	0.51 (0.68)

Intrusion Type	$F_{(1, 76)} = 0.13$, $p = 0.72$
List Organisation	$F_{(1, 76)} = 0.38$, $p = 0.54$
Frontal Subgroup	$F_{(4, 76)} = 0.10$, $p = 0.36$
Intrusion Type x Frontal Subgroup Interaction	$F_{(4, 76)} = 0.58$, $p = 0.68$
List Organisation x Frontal Subgroup Interaction	$F_{(4, 76)} = 0.96$, $p = 0.43$
List Organisation x Intrusion Type Interaction	$F_{(1, 76)} = 0.44$, $p = 0.62$
List Organisation x Intrusion Type x Frontal Subgroup Interaction	$F_{(4, 76)} = 0.26$, $p = 0.90$

Ref 2.2: Monitoring Performance

	Orbital Mean (SD)	Medial Mean (SD)	L Lateral Mean (SD)	R Lateral Mean (SD)	Control Mean (SD)
Percentage Words Correctly Monitored	93.94 % (6.65)	81.67 % (18.30)	89.79 % (10.63)	91.67 % (4.71)	88.78 % (10.42)
Percentage Words Incorrectly Identified as Repeated	8.62 % (9.02)	11.32 % (14.80)	1.92 % (0.25)	5.24 % (3.14)	5.00 % (9.41)

Percentage Words Correctly Monitored	$F_{(4, 77)} = 1.21$, $p = 0.32$
Percentage Words Incorrectly Identified as Repeated	$F_{(4, 71)} = 1.50$, $p = 0.21$

Ref 2.3: Category Switches in Recall

	Orbital Mean (SD)	Medial Mean (SD)	L Lateral Mean (SD)	R Lateral Mean (SD)	Control Mean (SD)
N	11	8	8	7	50
Mean No. Unnecessary Category Switches per List	0.32 (0.38)	0.37 (0.28)	0.71 (0.94)	0.26 (0.29)	0.55 (0.44)
Blocked Lists	0.15 (0.23)	0.29 (0.45)	0.54 (0.94)	0.0 (0.00)	0.36 (0.39)
Random Lists	0.48 (0.70)	0.46 (0.35)	0.88 (0.97)	0.52 (0.57)	0.74 (0.69)

List Organisation	$F_{(1, 77)} = 2.46, p = 0.12$
Frontal Subgroup	$F_{(4, 77)} = 1.79, p = 0.14$
List Organisation x Frontal Subgroup Interaction	$F_{(4, 77)} = 0.38, p = 0.82$

Level 3 Analyses (Reported only following a significant level 1 analysis)

SMIM

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
3.1	Mean Correct Recall	N = 11 7.69 (3.70)	N = 25 6.68 (3.09)	$T_{(34)} = -0.65, p = 0.52$
3.2	Mean Recalls per Category (Max 4)	N = 11 2.39 (0.56)	N = 22 2.33 (0.47)	$T_{(31)} = -0.33, p = 0.74$

IMonly

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
4.1	Mean Correct Recall	N = 17 6.13 (3.59)	N = 19 7.70 (2.81)	$T_{(34)} = 1.35, p = 0.19$
4.2	Mean Recalls per Category (Max 4)	N = 14 2.26 (0.56)	N = 19 2.42 (0.45)	$T_{(31)} = 0.91, p = 0.37$

LLat

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
5.1	Mean Correct Recall	N = 13 8.30 (4.48)	N = 23 6.44 (2.55)	$T_{(34)} = -0.69, p = 0.50$
5.2	Mean Recalls per Category (Max 4)	N = 11 2.52 (0.65)	N = 22 2.27 (0.39)	$T_{(31)} = -1.42, p = 0.16$

RLat

Ref		Area Damaged Mean (SD)	Area Not Damaged Mean (SD)	T test result
6.1	Mean Correct Recall	N = 11 7.85 (2.35)	N = 25 6.50 (3.59)	$T_{(34)} = -1.38, p = 0.18$
6.2	Mean Recalls per Category (Max 4)	N = 11 2.47 (0.40)	N = 22 2.30 (0.54)	$T_{(31)} = -0.94, p = 0.36$

APPENDIX 6: Visual Organisation and Monitoring Test: Insignificant Analyses

Level 1 Analyses

Ref		ANOVA result
1.1	**Picture Organisation x Intrusion Type x Group ANOVA**	
	Picture Organisation x Intrusion Type Interaction	$F_{(1, 99)} = 0.01, p = 0.91$
	Picture Organisation x Group Interaction	$F_{(2, 99)} = 1.69, p = 0.19$
	Intrusion Type x Group Interaction	$F_{(2, 99)} = 0.55, p = 0.58$
	Picture Organisation x Intrusion Type x Group Interaction	$F_{(2, 99)} = 0.36, p = 0.70$

Level 2 Analyses

Ref		ANOVA result
2.1	**Picture Organisation x Intrusion Type x Frontal Subgroup ANOVA**	
	Picture Organisation x Intrusion Type Interaction	$F_{(1, 79)} = 0.02, p = 0.88$
	Picture Organisation x Subgroup Interaction	$F_{(2, 79)} = 2.24, p = 0.07$
	Intrusion Type x Subgroup Interaction	$F_{(2, 79)} = 0.35, p = 0.85$
	Picture Organisation x Intrusion Type x Subgroup Interaction	$F_{(2, 79)} = 1.29, p = 0.28$

Ref 2.2: Monitoring Performance

	Orbital Mean (SD)	Medial Mean (SD)	L Lateral Mean (SD)	R Lateral Mean (SD)	Control Mean (SD)
Percentage Words Correctly Monitored	96.67 % (3.36)	86.84 % (11.24)	95.34 % (5.19)	92.46 % (7.25)	94.54 % (5.17)
Percentage Words Incorrectly Identified as Repeated	3.97 % (3.05)	5.56 % (5.07)	17.78 % (24.42)	17.36 % (15.77)	7.88 % (9.68)

Percentage Words Correctly Monitored $F_{(4, 79)} = 1.68, p = 0.16$
Percentage Words Incorrectly Identified as Repeated $F_{(4, 47)} = 1.50, p = 0.21$

Level 3 Analyses (Reported only following a significant level 1 analysis)

SMIM

Ref		Area Damaged N = 12 Mean (SD)	Area Not Damaged N = 26 Mean (SD)	T test result
3.1	Mean Correct Recall	5.22 (1.45)	5.38 (1.61)	$T_{(36)} = 0.28$, $p = 0.78$
3.2	Mean Extra-List Intrusions	0.17 (0.23)	0.18 (0.30)	$T_{(36)} = 0.12$, $p = 0.91$
3.3	Mean Prior-List Intrusions	0.42 (0.28)	0.56 (0.47)	$T_{(36)} = 0.96$, $p = 0.34$

IMonly

Ref		Area Damaged N = 18 Mean (SD)	Area Not Damaged N = 20 Mean (SD)	T test result
4.1	Mean Correct Recall	5.17 (1.81)	5.48 (1.29)	$T_{(36)} = 0.62$, $p = 0.54$
4.2	Mean Extra-List Intrusions	0.22 (0.35)	0.13 (0.19)	$T_{(36)} = -1.17$, $p = 0.25$
4.3	Mean Prior-List Intrusions	0.61 (0.52)	0.42 (0.28)	$T_{(36)} = -1.38$, $p = 0.18$

LLat

Ref		Area Damaged N = 14 Mean (SD)	Area Not Damaged N = 24 Mean (SD)	T test result
5.1	Mean Correct Recall	5.45 (1.86)	5.26 (1.37)	$T_{(36)} = -0.34$, $p = 0.73$
5.2	Mean Extra-List Intrusions	0.15 (0.15)	0.18 (0.33)	$T_{(36)} = 0.38$, $p = 0.71$
5.3	Mean Prior-List Intrusions	0.45 (0.41)	0.55 (0.43)	$T_{(36)} = 0.68$, $p = 0.50$

RLat

Ref		Area Damaged N = 11 Mean (SD)	Area Not Damaged N = 27 Mean (SD)	T test result
6.1	Mean Correct Recall	5.46 (1.13)	5.28 (1.70)	$T_{(36)} = -0.34$, $p = 0.74$
6.2	Mean Extra-List Intrusions	0.08 (0.13)	0.21 (0.31)	$T_{(36)} = 1.36$, $p = 0.18$
6.3	Mean Prior-List Intrusions	0.41 (0.29)	0.55 (0.46)	$T_{(36)} = 0.98$, $p = 0.34$

APPENDIX 7: Encoding Specificity Stimuli

Freq	Dimension	Target	Options (Correct answer in bold)
<10	ITS SHAPE	Rhubarb	**Leek**, Pumpkin
<10	MOST SIMILAR	Mushroom	Cupboard, Muscle, **Parsnip**, Pencil
>50	ITS COLOUR	Salt	Pepper, **Sugar**
<50	MOST SIMILAR	Garlic	Man, Kite, Abbey, **Vanilla**
>50	ITS COLOUR	Tin	Copper, **Silver**
>50	MOST SIMILAR	Bronze	Sparrow, **Aluminium**, Bubble, Rice
<10	ITS SIZE	Gorilla	**Bison**, Otter
<10	MOST SIMILAR	Wolf	Handle, Address, Fan, **Squirrel**
>50	ITS FUNCTION / WHAT IT IS FOR	Stool	Dresser, **Couch**
<10	MOST SIMILAR	Drawers	Dream, **Shelf,** Money, Soup
>50	NATURAL OR MAN-MADE?	Milk	Coke, **Water**
>50	MOST SIMILAR	Lemonade	Ribbon, Fish, **Coffee**, Face
>50	ITS SHAPE	Pan	Stove, **Bowl**
>50	MOST SIMILAR	Can Opener	**Mixer**, Van, Box, Plant
<10	ITS SHAPE	Watch	Cufflinks, **Bracelet**
<10	MOST SIMILAR	Necklace	**Bow-tie**, Bottle, Rock, Snake
>50	ITS COLOUR	Banana	**Lemon,** Tangerine
>50	MOST SIMILAR	Plum	Word, **Apricot**, Chess, Cap
>50	ITS SIZE	Toe	**Nose**, Hand
>50	MOST SIMILAR	Eye	Vase, Acid, Race, **Finger**
<10	NATURAL OR MAN-MADE?	Fur	**Leather**, Plastic
<10	MOST SIMILAR	Sheepskin	Peach, Kettle, Stair, **Suede**
<10	ITS FUNCTION / WHAT IT IS FOR	Fireplace	Skylight, **Radiator**
<10	MOST SIMILAR	Archway	Rope, **Pillar**, Seed, Teacher

APPENDIX 8: Encoding Specificity Task: Insignificant Analyses

Level 2 Analyses

Ref 2.1: Percentage Correct Recall Given Correct Encoding: Frontal Subgroup x Condition ANOVA

	Orbital Mean (SD)	Medial Mean (SD)	L Lateral Mean (SD)	R Lateral Mean (SD)	Control Mean (SD)
N	12	8	9	7	50
Correct Recall Specific Dimension Condition	67.00 (33.00)	56.00 (28.00)	61.00 (32.00)	59.00 (35.00)	73.00 (20.00)
Correct Recall Similar Condition	35.00 (24.00)	31.00 (31.00)	25.00 (20.00)	31.00 (8.00)	42.00 (20.00)

Condition	$F_{(1, 81)} = 72.85$, $p = 0.000$
Group	$F_{(4, 79)} = 1.15$, $p = 0.34$
Condition x Group Interaction	$F_{(4, 79)} = 0.68$, $p = 0.61$

Level 3 Analyses (Reported only following a significant level 1 analysis)

SMIM

Ref		Area Damaged N = 12 Mean (SD)	Area Not Damaged N = 26 Mean (SD)	T test result
3.1	Actual Correct Choices at Encoding (Specific Dimension Condition)	9.67 (4.54)	10.58 (4.40)	$T_{(36)} = 0.59$, $p = 0.56$
3.2	Correct Raw Recall / 15 (Specific Dimension Condition)	6.58 (4.40)	8.03 (3.78)	$T_{(36)} = 1.05$, $p = 0.30$
3.3	Correct Raw Recall / 15 (Similar Condition)	3.83 (3.04)	4.11 (2.58)	$T_{(36)} = 0.30$, $p = 0.77$
3.4	Correct Recall Given Correct Encoding (Specific Dimension Condition)	44.81 (37.34)	60.20 (30.87)	$T_{(36)} = 1.34$, $p = 0.19$
3.5	Correct Recall Given Correct Encoding (Similar Condition)	24.03 (20.79)	29.12 (22.23)	$T_{(36)} = 0.67$, $p = 0.51$
3.6	Percentage New Intrusions (Similar Condition)	15.64 (22.06)	8.02 (11.18)	$T_{(13.68)} = -1.13$, $p = 0.28$

IMonly

Ref		Area Damaged N = 18 Mean (SD)	Area Not Damaged N = 20 Mean (SD)	T test result
4.1	Actual Correct Choices at Encoding (Specific Dimension Condition)	9.83 (4.42)	10.70 (4.46)	$T_{(36)} = 0.60$, $p = 0.55$
4.2	Correct Raw Recall / 15 (Specific Dimension Condition)	7.44 (4.23)	7.70 (3.85)	$T_{(36)} = 0.19$, $p = 0.85$
4.3	Correct Raw Recall / 15 (Similar Condition)	4.11 (3.03)	3.95 (2.44)	$T_{(36)} = -0.18$, $p = 0.86$
4.4	Correct Recall Given Correct Encoding (Specific Dimension Condition)	58.24 (33.87)	52.74 (33.50)	$T_{(36)} = -0.50$, $p = 0.62$
4.5	Correct Recall Given Correct Encoding (Similar Condition)	29.84 (26.40)	25.42 (16.70)	$T_{(36)} = -0.62$, $p = 0.54$
4.6	Percentage New Intrusions (Similar Condition)	8.26(12.67)	12.38 (17.87)	$T_{(36)} = 0.81$, $p = 0.42$

LLat

		Area Damaged N = 14 Mean (SD)	Area Not Damaged N = 24 Mean (SD)	T test result
5.1	Actual Correct Choices at Encoding (Specific Dimension Condition)	9.36 (4.99)	10.83 (4.04)	$T_{(36)} = 1.00$, $p = 0.33$
5.2	Correct Raw Recall / 15 (Specific Dimension Condition)	7.35 (4.03)	7.71 (4.04)	$T_{(36)} = 0.26$, $p = 0.80$
5.3	Correct Raw Recall / 15 (Similar Condition)	3.79 (3.36)	4.17 (2.30)	$T_{(36)} = 0.42$, $p = 0.68$
5.4	Correct Recall Given Correct Encoding (Specific Dimension Condition)	51.66 (38.77)	57.49 (30.41)	$T_{(36)} = 0.52$, $p = 0.61$
5.5	Correct Recall Given Correct Encoding (Similar Condition)	24.19 (21.57)	29.45 (21.90)	$T_{(36)} = 0.72$, $p = 0.48$
5.6	Percentage New Intrusions (Similar Condition)	12.08 (19.44)	9.47 (13.16)	$T_{(36)} = -0.49$, $p = 0.62$

RLat

Ref		Area Damaged N = 11 Mean (SD)	Area Not Damaged N = 27 Mean (SD)	T test result
6.1	Actual Correct Choices at Encoding (Specific Dimension Condition)	11.00 (4.00)	10.00 (4.60)	$T_{(36)} = -0.63$, $p = 0.53$
6.2	Correct Raw Recall / 15 (Specific Dimension Condition)	9.09 (3.39)	6.96 (4.10)	$T_{(36)} = -1.52$, $p = 0.14$
6.3	Correct Raw Recall / 15 (Similar Condition)	4.73 (2.15)	3.74 (2.88)	$T_{(36)} = -1.02$, $p = 0.31$
6.4	Correct Recall Given Correct Encoding (Specific Dimension Condition)	58.74 (31.54)	53.96 (34.52)	$T_{(36)} = -0.40$, $p = 0.69$
6.5	Correct Recall Given Correct Encoding (Similar Condition)	31.75 (13.15)	25.78 (24.28)	$T_{(32.76)} = -0.97$, $p = 0.34$
6.6	Percentage New Intrusions (Similar Condition)	6.97 (7.37)	11.84 (17.79)	$T_{(35.93)} = 1.19$, $p = 0.24$

APPENDIX 9: Reality Monitoring Task Stimuli

Read Aloud	Prompted to Imagine	(Correct Answer)	Distractor
Copper	A Metal: I	(Iron)	Steel
Basketball	A Sport: F	(Football)	Baseball
Magazine	Something you Read: B	(Book)	Newspaper
Wool	A Type of Fabric: C	(Cotton)	Silk
Knife	A Kitchen Utensil: F	(Fork)	Spoon
Maple	A Tree: O	(Oak)	Pine
Synagogue	A Religious Building: C	(Church)	Temple
Whiskey	An Alcoholic Drink: B	(Beer)	Gin
Orange	A Fruit: A	(Apple)	Pear
Hill	A Natural Feature: M	(Mountain)	Valley
Rifle	A Weapon: G	(Gun)	Bomb
Robin	A Bird: S	(Sparrow)	Cardinal
Saw	A Tool: H	(Hammer)	Nails
Classical	A Type of Music: J	(Jazz)	Rock
Ball	A Toy: D	(Doll)	Car

APPENDIX 10: Reality Monitoring Task: Insignificant Analyses

Level 3 Analyses (Reported only following a significant level 1 analysis)

SMIM

Ref		Area Damaged N = 11 Mean (SD)	Area Not Damaged N = 25 Mean (SD)	T test result
1.1	Imagined Correct Responses	7.27 (4.15)	8.12 (3.55)	$T_{(34)} = 0.63$, $p = 0.54$

IMonly

Ref		Area Damaged N = 17 Mean (SD)	Area Not Damaged N = 19 Mean (SD)	T test result
2.1	Imagined Correct Responses	7.35 (3.67)	8.32 (3.77)	$T_{(34)} = 0.77$, $p = 0.44$

LLat

Ref		Area Damaged N = 13 Mean (SD)	Area Not Damaged N = 23 Mean (SD)	T test result
3.1	Imagined Correct Responses	8.00 (3.08)	7.78 (4.07)	$T_{(36)} = -0.17$, $p = 0.87$

RLat

Ref		Area Damaged N = 11 Mean (SD)	Area Not Damaged N = 25 Mean (SD)	T test result
4.1	Imagined Correct Responses	9.55 (3.17)	7.12 (3.73)	$T_{(34)} = -1.87$, $p = 0.07$

APPENDIX 11: Continuous Recognition Task: Insignificant Analyses

Level 3 Analyses (Reported only following a significant level 1 analysis)

Ref 1.1 Hit Rate: SMIM x Run ANOVA

	Area Damaged N = 11 Mean (SD)	Area Not Damaged N = 26 Mean (SD)
Hit Rate Run 1	20.00 (9.32)	21.96 (9.35)
Hit Rate Run 2	15.09 (8.57)	17.96 (8.55)
Hit Rate Run 3	19.45 (7.89)	22.08 (7.59)

Run	$F_{(1.69, 70)} = 10.22$, $p = 0.000$, Greenhouse Geisser correction
SMIM	$F_{(1, 35)} = 0.74$, $p = 0.40$
Run x SMIM interaction	$F_{(1.69, 70)} = 0.07$, $p = 0.91$, Greenhouse Geisser correction

Ref 1.2 Hit Rate: IMOnly x Run ANOVA

	Area Damaged N = 17 Mean (SD)	Area Not Damaged N = 20 Mean (SD)
Hit Rate Run 1	21.88 (8.40)	20.95 (10.12)
Hit Rate Run 2	17.53 (7.57)	16.75 (9.47)
Hit Rate Run 3	22.47 (5.52)	20.30 (9.14)

Run	$F_{(1.68, 70)} = 11.83$, $p = 0.000$, Greenhouse Geisser correction
IMOnly	$F_{(1, 35)} = 0.07$, $p = 0.79$
Run x IMOnly interaction	$F_{(1.68, 70)} = 0.19$, $p = 0.79$, Greenhouse Geisser correction

Ref 1.3 Hit Rate: LLat x Run ANOVA

	Area Damaged N = 13 Mean (SD)	Area Not Damaged N = 24 Mean (SD)
Hit Rate Run 1	19.23 (11.29)	22.54 (7.97)
Hit Rate Run 2	18.92 (7.60)	16.13 (9.01)
Hit Rate Run 3	22.54 (7.28)	20.63 (7.94)

Run	$F_{(2, 70)} = 9.43$, $p = 0.000$
LLat	$F_{(1, 35)} = 0.15$, $p = 0.70$
Run x LLat interaction	$F_{(2, 70)} = 1.97$, $p = 0.15$

Ref 1.4 Hit Rate: RLat x Run ANOVA

	Area Damaged N = 12 Mean (SD)	Area Not Damaged N = 25 Mean (SD)
Hit Rate Run 1	21.67 (9.87)	21.24 (9.15)
Hit Rate Run 2	15.92 (9.97)	17.68 (7.93)
Hit Rate Run 3	19.67 (9.23)	22.08 (6.87)

Run	$F_{(1.69, 70)} = 10.70$, $p = 0.000$, Greenhouse Geisser correction
RLat	$F_{(1, 35)} = 0.30$, $p = 0.59$
Run x RLat interaction	$F_{(1.69, 70)} = 0.36$, $p = 0.67$

Ref 1.5 False Positive Rate: SMIM x Run ANOVA

	Area Damaged N = 10 Mean (SD)	Area Not Damaged N = 26 Mean (SD)
False Positive Rate Run 1	5.18 (4.92)	6.12 (5.64)
False Positive Rate Run 2	8.90 (5.04)	8.27 (7.36)
False Positive Rate Run 3	8.27 (6.20)	9.42 (9.49)

Run	$F_{(2, 68)} = 3.73, p = 0.03$
SMIM	$F_{(1, 34)} = 0.03, p = 0.87$
Run x SMIM interaction	$F_{(2, 68)} = 0.15, p = 0.86$

Ref 1.6 False Positive Rate: IMOnly x Run ANOVA

	Area Damaged N = 17 Mean (SD)	Area Not Damaged N = 19 Mean (SD)
False Positive Rate Run 1	5.82 (6.23)	5.85 (4.72)
False Positive Rate Run 2	8.59 (7.94)	8.32 (5.66)
False Positive Rate Run 3	10.47 (10.96)	7.90 (5.92)

Run	$F_{(2, 68)} = 4.61, p = 0.01$
IMOnly	$F_{(1, 34)} = 0.25, p = 0.62$
Run x IMOnly interaction	$F_{(2, 68)} = 0.71, p = 0.49$

Ref 1.7 False Positive Rate: LLat x Run ANOVA

	Area Damaged N = 13 Mean (SD)	Area Not Damaged N = 23 Mean (SD)
False Positive Rate Run 1	6.46 (7.10)	5.50 (4.32)
False Positive Rate Run 2	10.69 (8.01)	7.17 (5.69)
False Positive Rate Run 3	9.85 (8.37)	8.67 (8.84)

Run	$F_{(2, 68)} = 4.39, p = 0.02$
LLat	$F_{(1, 34)} = 0.76, p = 0.39$
Run x LLat interaction	$F_{(2, 68)} = 0.79, p = 0.46$

Ref 1.8 False Positive Rate: RLat x Run ANOVA

	Area Damaged N = 11 Mean (SD)	Area Not Damaged N = 25 Mean (SD)
False Positive Rate Run 1	6.92 (4.98)	5.32 (5.59)
False Positive Rate Run 2	8.73 (6.77)	8.32 (6.85)
False Positive Rate Run 3	6.75 (5.24)	10.20 (9.68)

Run	$F_{(2, 68)} = 2.31, p = 0.11$
RLat	$F_{(1, 34)} = 0.03, p = 0.86$
Run x RLat interaction	$F_{(2, 68)} = 2.03, p = 0.14$